

MOGENS MØLLER

Ventricular arrhythmias following myocardial infarction

**Incidence and prognostic importance
studied by repeated 24-hour
electrocardiographic monitoring**



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PREFACE

The present study was undertaken in the period 1978-79 during my employment as a research fellow at the Department of Clinical Physiology and in close co-operation with Medical Department B, Odense University Hospital.

Bent Lyager Nielsen, M.D., encouraged me to carry out the investigation and professor Jørgen Fabricius, M.D., made it possible by creating excellent working conditions. Both of them followed my work with the greatest interest.

Torben Haghfelt, M.D., introduced me to the problem of sudden death. I have benefitted from discussions with Per Thayssen, M.D. and Johannes Stræde Nielsen, M.D., Per Arnsbo, engineer, gave me technical advice and Lise Hansen, cand. scient., carried out the data processing.

Secretary Karen Eckhoff was a great help during the period of investigation, and Birgit Bruhn Lorenzen, secretary, typed the final manuscript.

Competent assistance was given by the staff members of the Department of Clinical Physiology and the Coronary Care Unit of the Medical Department B.

C.N. Harris, B. Sc., Ph. D., translated the manuscript.

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Finally I would like to thank Kirsten, Jens and Kristian Møller for their indulgence and encouragement during my work.

This dissertation was submitted to the Medical Faculty of The Odense University on April 29th, 1980.

Odense February 1981.

Mogens Møller.

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ABBREVIATIONS USED

AMI	:	Acute myocardial infarction
A-V	:	Atrio-ventricular
CCU	:	Coronary care unit
CK	:	Creatine kinase
ECG	:	Electrocardiogram
FAC	:	First ambulatory control
LAH	:	Left anterior hemiblock
LBbB	:	Left bundle branch block
LHP	:	Late hospital phase
LPH	:	Left posterior hemiblock
NS	:	Not significant
RBbB	:	Right bundle branch block
S-A	:	Sino-atrial
SAC	:	Second ambulatory control
SCD	:	Sudden cardiac death
SVEB	:	Supraventricular ectopic beat
SVT	:	Supraventricular tachycardia
TAC	:	Third ambulatory control
VA	:	Ventricular arrhythmia
VEB	:	Ventricular ectopic beat
VF	:	Ventricular fibrillation
VT	:	Ventricular tachycardia

CHAPTER I : INTRODUCTION

The increasing use during the last decades of mobile and stationary coronary care units with continuous electrocardiographic monitoring has improved our knowledge of the type and incidence of arrhythmias during the acute phase of a myocardial infarction. Experience gained from the mobile coronary care units (Adgey et al. 1971, Haghfelt 1976) has indicated a high incidence of bradyarrhythmias in particular, but also ventricular tachyarrhythmias in the first few hours after the onset of the infarction. Careful, continuous electrocardiographic monitoring during the hospital phase of a myocardial infarction has demonstrated ventricular arrhythmias in almost all of these patients (Julian et al. 1964, Mogensen 1970, Romhilt et al. 1973), and treatment with antiarrhythmic drugs and electric defibrillation has reduced the lethality from arrhythmias in patients with acute myocardial infarction (Lown et al. 1967, Christiansen et al. 1971).

The most important problem, however, is that the majority of deaths from ischaemic heart disease occur suddenly outside the hospital (Kuller et al. 1966) and thus result in unsolved prophylactic and therapeutic problems. A rational approach to the problem would be the prevention of ischaemic heart disease, but no striking results have been achieved to date in this respect, even though a later report would suggest that the occurrence of cardiac death is decreasing in the U.S.A. (Cooper et al. 1978). A step that could be taken in the mean time would be to prevent sudden cardiac death, and as this is presumed to be caused mainly by ventricular fibrillation (Lown et al. 1975, Julian 1976), the treatment would therefore be prophylactic measures designed to counteract factors producing arrhythmias and arrhythmias per se.

Epidemiological studies have demonstrated that the presence of ventricular ectopic beats recorded on a resting electrocardiogram (Chiang et al. 1969) or during six hours of electrocardiographic monitoring (Hinkle et al. 1969) indicate an increased risk of sudden cardiac death in persons both with and without symptoms of cardiac disease, while ventricular ectopic beats on a resting electrocardiogram in a later investigation were of no prognostic significance (Fisher & Tyroler 1973).

The presence of ventricular ectopic beats on a resting

electrocardiogram recorded from 2035 men between the ages of 35 and 60 years, in a placebo-treated group of post-infarction⁷ patients, was found to be connected with twice the risk of sudden cardiac death during the three years observation period, as compared to those without ventricular ectopic beats (Coronary Drug Project Research Group 1973). Sudden cardiac death occurred in particular among patients with frequent ventricular ectopic beats, runs of ventricular ectopic beats and R on T phenomenon. Similar findings have been reported by Ruberman et al. (1977) in an investigation comprising 1739 men with a previous myocardial infarction and with an electrocardiogram of 60 minutes duration recorded within the first year after the infarction. During a follow-up period of three years the risk of sudden cardiac death was three to five times higher in patients with complicated ventricular ectopic beats (multiform, pairs, runs, R on T) as compared to the other patients, while uniform ventricular ectopic beats were not connected with an increased risk irrespective of their number. Complicated ventricular ectopic beats were found to be the most important prognostic factor per se, followed by cardiac failure and ST-segment depression at the time of examination.

The introduction of long-term electrocardiographic monitoring by means of a small portable tape-recorder (Holter 1961) has provided improved facilities for studying arrhythmias after the technical problems in connection with the weight

of the tape-recorder and its function were solved in the early 1970's, and after a solution has been found to the analytical problems during the last three to four years. A number of investigations regarding the occurrence of arrhythmias during the late hospital phase of an acute myocardial infarction have been carried out using six hours of telemetry (Rehnqvist 1976) or electrocardiographic tape-recording of one to twenty-four hours duration (Moss et al. 1971, Van Durme 1975, Vismara et al. 1975, Moss et al. 1977, Schulze et al. 1977, Abjörn et al. 1977, Federman et al. 1978), and have contributed to a better knowledge of the occurrence of various forms of ventricular arrhythmias during this phase. Several investigations (Van Durme 1975, Vismara et al. 1975, Moss et al. 1977, Rehnqvist et al. 1978), however, suggest that the presence of frequent ventricular ectopic beats and particularly ventricular ectopic beats occurring from more than one focus, occurring repetitively or as R on T phenomenon, significantly increase the risk of sudden cardiac death, but to date it has been impossible to indicate any well-defined high risk group by means of the arrhythmia pattern, even though Lown et al. (1975) in particular consider that ventricular arrhythmias, as an expression of electrical instability of the myocardium, are a prognostically unfavourable factor per se.

In a recent investigation by Humphries et al. (1978) of 81 patients in the late hospital phase of a myocardial infarction, the results of 24-hour electrocardiographic tape-recording and coronary arteriography were compared. Complicated ven-

tricular ectopic beats (multiform, paired, ventricular tachycardia, R on T) occurred in 24 of 54 patients with at least 50% stenosis of two or three of the large coronary arteries as compared to two of the remaining 27 patients. The investigation also showed that 11 of 20 patients with an ejection fraction (the percentage of the left ventricular diastolic volume expelled during the systole) of less than 40% had complicated ventricular arrhythmias against 15 of 59 patients with an ejection fraction greater than 40%. Nine cases of sudden cardiac death occurred in an average follow-up period of 18 months. The report does not give the exact haemodynamic or electrocardiographic findings in these patients, but it is stated that sudden cardiac death was particularly prevalent in patients with stenosis of three coronary arteries, together with a low ejection fraction and complicated ventricular arrhythmias.

In the posthospital phase the arrhythmia pattern has been studied using both resting electrocardiograms (Coronary Drug Project Research Group 1973) as well as ambulatory electrocardiographic tape-recording of one to twenty-four hours duration (Kotler et al. 1973, Myburgh & Gelder 1974, Ruberman et al. 1977, Vorpahl & Blümchen 1978), and a few authors have studied patients with infarction during both the hospital and posthospital phases in prospective investigations (Van Durme 1975, Moss et al. 1977, Rehnqvist & Sjögren 1977, Federman et al. 1978). These investigations have been carried out at various time after onset of the

infarction and using various durations of monitoring, and, in the main, without the use of arrhythmia computers, as is possible today.

In general, the investigations suggest that the pattern of ventricular arrhythmias is comparatively constant during the first months after an infarction, but with considerable individual variation.

The electrophysiology in respect of the occurrence of ventricular arrhythmias is only partially known, and present knowledge is based mainly on animal experimental studies. Two different electrophysiological mechanisms are considered as playing a part: 1) a so-called "re-entry" phenomenon, contingent on a local unidirectional conduction block, a delayed activation of the tissue beyond the block due to transmission via an alternative pathway, further delay while passing the block itself and subsequent re-activation of tissue proximal to the block while in the resting phase with resulting ectopic depolarization. 2) an enhanced automaticity with a subsequent diastolic depolarization. Both of these mechanisms are described in detail in a survey by Witt & Bigger (1975). During the first half to one hour after an experimental myocardial infarction, the ventricular arrhythmias are considered as being brought about by the "re-entry" phenomenon. After which there is a phase of 12-24 hours with only slight ectopic activity, followed by a phase marked by arrhythmias due to the enhanced automaticity. The arrhythmias

days to weeks after an experimental infarction are thought to be caused by the "re-entry" phenomenon. To what extent these animal experimental results may be applied to human myocardial infarction is unknown, but the introduction of programmed electrical stimulation in the right ventricle (Wellens et al. 1972) has contributed to the evaluation of a number of electrophysiological and pharmacological aspects in patients with ventricular tachycardia. The studies suggest that ventricular arrhythmias in the phase of an infarction comprising the object of the present study result from "re-entry" (Josephson et al. 1978).

Prophylactic measures designed to prevent sudden cardiac death after a myocardial infarction have been studied in a number of pharmacological investigations, using difenylhydantoin (Collaborative Group 1971), and procainamide (Kosowsky et al. 1973, Lyager Nielsen et al. 1978) and have given disappointing results. On the other hand, treatment with adrenergic beta-receptor blocking agents in later investigations have produced encouraging results (Wilhelmsson et al. 1974, Multicentre International Study 1975, Andersen et al. 1979), even though an early study demonstrated no effect on the occurrence of sudden cardiac death (Reynolds & Whitlock 1972). It should be mentioned in this connection, that present experience would suggest that aorto-coronary by-pass surgery does not reduce the occurrence of ventricular arrhythmias

in patients with ischaemic heart disease (Tilkian et al. 1976, Guinn & Mathur 1977, Leutenegger et al. 1979).

The present investigation has been designed to describe the occurrence of ventricular arrhythmias during the first six months after a myocardial infarction, where the occurrence of cardiac death is particularly high (Thygesen et al. 1974). Further to determine the feasibility of employing the pattern of arrhythmias for segregating patients liable to succumb to sudden cardiac death.

The investigation has been based on the use of equipment for 24-hour ambulatory electrocardiographic monitoring by means of a small portable tape-recorder and the use of an arrhythmia computer for the qualitative and quantitative evaluation of ventricular ectopic beats.

The object of the investigation has been:

- 1) to describe the occurrence of ventricular arrhythmias at four different times during the first six months after an acute myocardial infarction.
- 2) to describe ventricular arrhythmias, qualitatively and quantitatively.
- 3) to describe the diurnal variation in ventricular arrhythmias.
- 4) to describe ventricular arrhythmias in relation to a number of clinical parameters in the acute and chronic phases of myocardial infarction.
- 5) to evaluate the long-term prognostic significance of ventricular arrhythmias.

CHAPTER II : METHODS

Selection criteria

The investigation comprises the first 100 patients discharged from the Medical Department B of the Odense University Hospital, after the 1st of January 1978, following admission for an acute myocardial infarction according to the criteria of the World Health Organization (1971).

The following patients were excluded from the investigation:

- 1) patients 70 years of age or more at the time of admission.
- 2) patients resident outside the county of Funen.
- 3) patients with severe chronic or malignant disease.
- 4) patients employed by the hospital authorities or their near relatives.
- 5) patients refusing to participate.

- 6) patients born on the 3rd, 5th, 6th, 13th, 21st, 22nd, and 26th of a month.

The latter criterion was employed owing to the fact that only four tape-recorders were available. The criteria for inclusion in the study remained unchanged during the period of investigation.

Patient information

A patient complying with the admission criteria and expected to be discharged alive was given verbal and written information regarding the scientific character and object of the investigation. If the patient consented to participate, the general practitioner was advised of the follow-up programme.

Design of the study

The patients were subjected to four examinations. The first took place shortly before discharge, the others approximately one, three and six months after the infarction. In addition, follow-up was carried out 12 months and approximately 18 months (15-22 months) after the initial infarction.

Hospital phase

The patients were primarily admitted to the coronary care unit of the University Hospital and connected to the central electrocardiographic monitoring system.

A resting electrocardiogram was taken using 12 leads on arrival. Blood samples were also withdrawn for the determination of the enzymes creatine kinase, aspartate aminotransferase and lactic dehydrogenase. These tests were repeated daily.

The electrocardiographic monitoring in the coronary care unit was carried out by means of a single lead. The electrocardiogram could be observed on an oscilloscope above the patient's bed and also in the central station. All the electrocardiograms were recorded continuously on magnetic tapes. A frequency based alarm system with automatic electrocardiographic print-out, when the heart rate exceeded preset limits, was employed. Computerized electrocardiographic analysis was not employed in the coronary care unit during the period of the present investigation. The arrhythmias observed were noted on a special form.

The duration of the central electrocardiographic monitoring depended on the character of the arrhythmias and the clinical condition of the patient. After cessation of the continuous monitoring, the patient was either retained in the coronary care unit or transferred to another ward in the same building. The medical staff and principles of treatment were identical in these departments. Ventricular arrhythmias were treated with intravenous lidocaine when the ventricular ectopic beats comprised more than 10% of the QRS complexes, occurred as

R on T phenomena or were repetitive. Beta-blocking agents or procainamide given intravenously were employed when lidocaine was ineffective.

Ventricular arrhythmias during the acute phase were not routinely treated with oral antiarrhythmic agents following the discontinuation of the intravenous therapy. In cases where oral treatment was considered necessary, beta-blocking agents, quinidine or procainamide were used.

A temporary transvenous pace-catheter was used in cases of 3rd degree atrio-ventricular block as well as 2nd degree Mobitz' type II block, and in cases of sinus arrest with ventricular asystolia of more than three to four seconds duration.

Heart failure was treated with diuretics, eventually combined with digoxin. An X-ray of the chest was taken as required, at least once during the admission.

Investigations during the late hospital phase

A review of the case records was carried out just prior to discharge, when a patient complied with the inclusion criteria. Blood samples were withdrawn for se-electrolyte, se-creatinine and hemoglobin determinations, and a clinical examination carried out together with the recording of a resting electrocardiogram employing 12 leads over a period of 60 seconds. A 24-hour electrocardiographic tape-recording was started following this with the patient fully mobilized.

Follow-up period

The patients were examined by the author approximately one, three and six months after discharge, where the case history was reviewed and a clinical examination carried out. A resting electrocardiogram of 60 seconds duration was recorded followed by 24-hour ambulatory electrocardiographic monitoring during normal activity. Serum electrolyte determination and a chest X-ray were carried out at the six months control examination, and if indicated at one and three months examination.

The continued treatment of the patients during the follow-up period was that normally employed, no regard being taken to the results of the 24-hour monitoring. On the other hand, any prescribed drugs were not discontinued during the 24-hours of monitoring.

The National Registration Office was contacted 12 and 15 - 22 months (median 18 months) after the initial infarction in order to ascertain, whether the patient was still alive. If this was not so, information regarding the time and cause of death was obtained from the next-of-kin, emergency room or hospital records and confirmed by the death certificate or autopsy report. All living patients were contacted by post or telephone, and in cases of re-admission to hospital the necessary hospital records reviewed.

REGISTRATION METHODS

Resting electrocardiogram

A daily resting electrocardiogram was recorded during admission to the coronary care unit employing a three channel mingograph 31 (Elema-Schönander) using leads I, II, III, aVR, aVL, aVF and $V_1 - V_6$. A paper speed of 50 mm/second and a test signal of 1 mV = 10 mm were used. All resting electrocardiograms were recorded with the patient in the supine position.

Electrocardiographic tape-recording

A diagram of the principle is shown in figure 1.

Tape-recorder

A Medilog 4-24 tape-recorder (Oxford Instruments Ltd.) with amplifiers for electrocardiographic recording in two leads and with time and event marking was employed. The tape speed was 2 mm/second, the weight approximately 400 grams and the size 112 x 87 x 36 mm. The tape-recorder was borne in a leather bag attached to a belt or in a shoulder strap. The 3 db band-width was 0.2 - 100 Hz on recording but the upper limit was reduced to 35 Hz during processing in the arrhythmia analyser (real time). The time marking was a quartz crystal controlled 60 Hz sinus modulation and the event marking a simultaneous 30 Hz modulation on the same track.

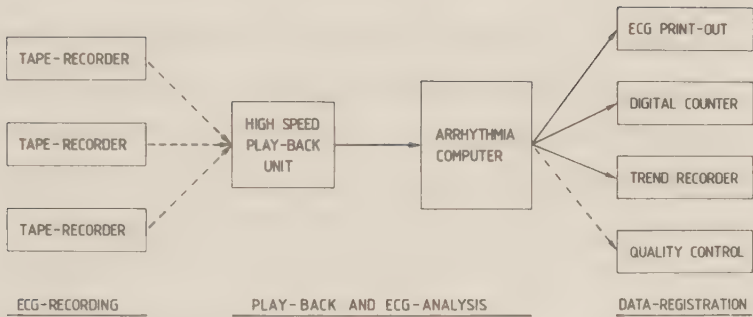


Figure 1

A diagram of the principle set-up of the equipment employed for ambulatory electrocardiographic monitoring

Each tape-recorder ran on four mercury batteries (Mallory Duracell RM-IN), which were found to maintain an almost constant voltage for 88 hours. Each battery was only used for two times 24 hours. The tapes employed were cassette tapes of the type C-120 (Philips).

Electrodes

Electrodes of the adhesive disposable type, silver/silver chloride were employed. The skin was carefully cleaned and abraded prior to attachment. The electrodes of one lead were placed above the sternum and at the position of V_3 , those of the other lead above the sternum and at the position of V_6 . Initially the electrocardiographic signal was tested at the start of each monitoring using an oscilloscope, later this was mainly employed for obese patients, and in cases where the resting electrocardiogram had shown bundle branch block or QRS complexes of low amplitude. The tests included various electrode positions and the patient in various positions.

Play-back unit

A PB-2 playback unit (Oxford Instruments Ltd.) was used with a play-back speed of 120 mm/sec, corresponding to 60 times real time. The play-back took place in two leads with simultaneous digital time display.

Arrhythmia analyser

The analyser was a RME-Pathfinder high speed ECG analy-

ser (Reynolds Medical Electronics Ltd.). The analysis of only one electrocardiographic lead at a time could be carried out, but it was possible to switch from one lead to the other.

The morphology of the patient's normal QRS complex was entered into the analogue/hybrid memory of the instrument in a 200 msec wide window. The principle of the analysis was a comparison of the morphology of each QRS complex with the memorized normal complex, as shown in figure 2. Thereafter the greatest acceptable difference in morphology before a QRS complex is termed aberrant was preset on the analyser. A combination of aberrant classification and prematurity were used for the determination of ventricular ectopic beats.

The analyser permitted the selection of a number of electrocardiographic abnormalities, which were automatically registered. On the whole, these were 1) normal, premature QRS complexes with adjustable marking of the prematurity, 2) consecutive, normal QRS complexes between two and nine with a coupling interval from 400 - 600 msec (i.e. supraventricular tachycardia), 3) aberrant QRS complexes, 4) aberrant, premature QRS complexes with adjustable marking of the prematurity, 5) consecutive aberrant QRS complexes between two and ten with a coupling interval from 400 - 600 msec (i.e. ventricular tachycardia), 6) R on T phenomenon with adjustable marking of the end of the T wave, 7) R-R intervals exceeding a preset value within the range 500 - 2500 msec.

On the occurrence of electrocardiographic abnormalities, the electrocardiogram could be retained on the oscilloscope for a 10 - 40 second real time sequence, and the electrocardiogram could, at the same time, be recorded automatically at a paper speed of 25 mm/sec in sequences of 10 - 40 seconds duration.

Arrhythmia registration

General remarks on the principle

The occurrence of arrhythmias during each tape-recording was studied by analysing each tape at least twice. All the analyses were carried out by the author. Initially, some brief sequences of the tape were analysed in order to evaluate the morphology of normal QRS complexes, as well as of any possible ectopic beats. A normal complex was then entered into the memory of the arrhythmia analyser. Thereafter the first play-back of the whole tape was carried out employing the automatic function of the apparatus. The electrocardiographic signal on the built-in oscilloscope were kept under observation. The apparatus was initially adjusted to detect brady-arrhythmias. In order to obtain an impression of the patient's heart rate/min and the occurrence of ventricular ectopic beats throughout the 24 hour period, trend curves of these parameters were drawn during the first play-back. The analyser equipment was connected to a Hewlett Packard XY-plotter 7064A via the analogue output. The output for

Computer detection of ventricular ectopic complexes

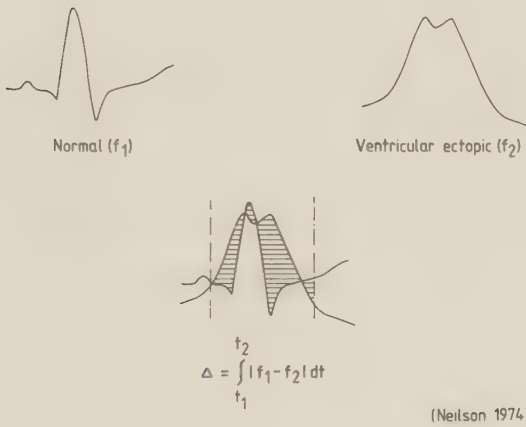


Figure 2

The principle employed for comparing the morphology of QRS complexes during arrhythmia analysis.

After Neilson (1974)

heart rate/min and the number of ventricular ectopic beats/min was a voltage from 0 to +5 volts, representing 0 to 200 beats/min. One cm of the X-axis of the plotter corresponded to 50 minutes real time. An example of a trend curve is shown in figure 3.

After the initial analysis the instrument was optimally adjusted for the subsequent quantitative analysis of the ventricular ectopic beats. At the same time, the tapes, which due to the technical quality, the presence of intermittent QRS changes, or high T waves, were unusable, were discarded in respect of the automatic analysis. These tapes were analysed employing a combination of automatic analysis and manual play-back, possibly with long sequences recorded on paper by means of a jet ink writer, as described under quality control. The other tapes (approximately 90%) were analysed using the arrhythmia computer with particular adjustment of the various functions for the detection of ventricular arrhythmias. All cases of repetitive ventricular ectopic beats and R on T phenomena were recorded on paper employing real time. At least one beat from each focus was recorded in real time in cases of multiform ventricular ectopic beats.

In cases where the tape contained many ventricular ectopic beats or repetitive ventricular ectopic beats at short intervals, recordings of long sequences were made on paper, and in a number of cases the tape was analysed several times.

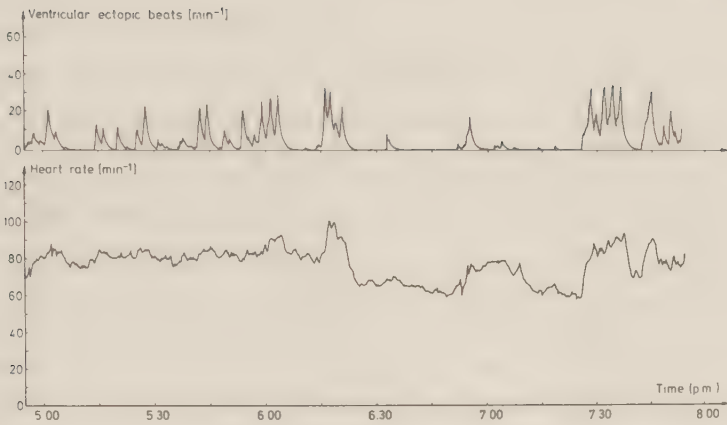


Figure 3

A trend curve over the number of ventricular ectopic beats per minute (upper) and the average heart rate per minute (lower)

Four digital counters (Reynolds Medical Electronics Ltd.) were employed for quantitative arrhythmia registration; these were coupled to the logic output of the analysis apparatus. It was possible during each analysis to simultaneously register four of the mentioned electrocardiographic parameters.

The 24 hours of each monitoring were divided into four periods of six hours, and a summary made of the ventricular arrhythmias in each period. The registration included the number of ventricular ectopic beats, repetitive ventricular ectopic beats (which were subdivided using the real time recordings) as well as R on T phenomena.

The quantitative analysis was supplemented with registration of the occurrence of ventricular ectopic beats as bigeminy or from several foci, similarly the ventricular arrhythmias were classified using a modified Lown & Wolf grading (1971) (see paragraph on definition).

Quality Control

The reproducibility of electrocardiographic analysis

The reproducibility was determined by selecting from the collection of tapes, five 24-hour recordings containing at least 100 ventricular ectopic beats. Each tape was analysed ten times following initial adjustment of the apparatus and employing the same adjustment each time. The grand mean with regard to the total number of QRS

complexes was 95.613 with a total SD of 137, while the corresponding count for ventricular ectopic beats was 1.013 with a total SD of 20.

The accuracy of electrocardiographic analysis

The accuracy of the analyses was evaluated on the basis of the first 500 recordings carried out with the equipment. The tapes in which one lead at least was not of good technical quality were excluded from the tape collection. Further, tapes with particularly high T waves or with intermittent bundle branch block, were also excluded as it is known from experience that these give unreliable results on automatic analysis. This exclusion included approximately 12% of the tapes. Twenty tapes were then selected from the remainder. Two periods of one hour were selected at random from each of these tapes for automatic analysis. The whole of the electrocardiogram was recorded during the analysis on a six channel jet ink recorder (Mingograph 81, Elema-Schönander) with a paper speed of 500 mm/sec, as shown in figure 4. The upper line shows the electrocardiogram, the next line normal QRS complexes marked via an impulse from the logic output of the analyser, the third line the ventricular ectopic beats similarly marked, and finally, the lower line shows marking of ventricular ectopic beats occurring as pairs.

After the automatic analysis the whole of the printout was evaluated manually. The total of 40 hours of real time electrocardiographic recordings contained, following manual classification, 13.369 ventricular ectopic beats.

A comparison with the automatic analysis revealed that the number of false negative ventricular ectopic beats was approximately 6%, while the number of false positive ventricular ectopic beats comprised approximately 2%. Between 69% and 100% of the ventricular ectopic beats were identified correctly in the individual hour.

The 40 hours real time analysis contained, following manual inspection, 211 episodes of repetitive ventricular ectopic beats. Of these 163 were correctly identified by the automatic analysis, corresponding to 77%, while the number of false positives was 5%. Most of the false negative episodes were on the same tape, and resulted from varying morphology of the first and second ventricular ectopic beat in connection with paired occurrence. No quality control was carried out in respect of the ability of the computer to detect other types of arrhythmias, and for this reason the incidence stated in the section on results are the number of episodes actually detected by the computer and verified on the oscilloscope or on print-out, and therefore a minimum.

DEFINITIONS

Acute myocardial infarction

The diagnostic criteria for definite acute myocardial infarction followed the World Health Organization (1971). The diagnosis is thus based on the case history, the daily electrocardiographic recording and enzyme determinations. Autopsy findings have been employed as diagnostic criteria during the follow-up period.

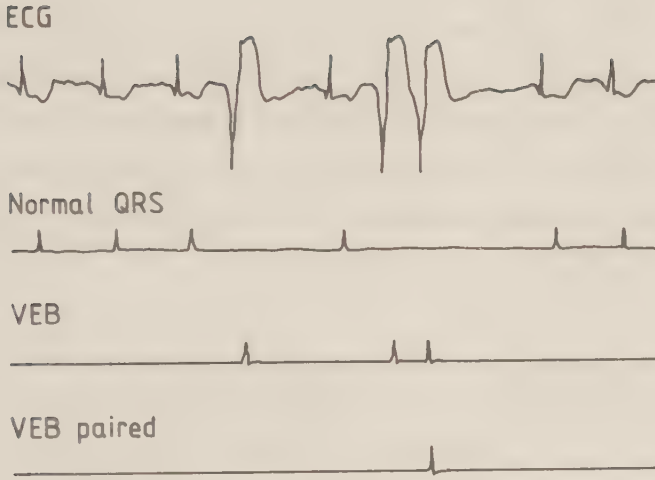


Figure 4

An example of the recording from a jet ink writer in connection with the evaluation of the accuracy of arrhythmia analysis. The upper line shows the electrocardiogram, while the markers in the other three lines indicate the classification by the computer of the individual QRS complexes as normal QRS complexes, ventricular ectopic beats and paired ventricular ectopic beats, respectively

Localization of the infarction

The localization was evaluated from the daily electrocardiograms. On the occurrence of typical electrocardiographic changes in leads I, aVL or V₁ to V₆, the infarction was termed anterior, and with typical changes in leads II, III and aVF, inferior. Provided the changes were present at both sites the term multiple has been employed. The term indefinite myocardial infarction was used in cases where it was impossible to determine the localization due, for example, to bundle branch block or previous myocardial infarction.

Type of infarction

Providing the criteria for the development of Q waves were present, the infarction was considered transmural. In those cases where the electrocardiographic changes occurred as development of negative T waves, present for more than 24 hours without the simultaneous development of Q waves, the infarction was termed subendocardial.

Angina pectoris

Stable angina pectoris was defined employing the criteria of the World Health Organization (1971), unstable angina pectoris as suggested by Chahine (1975).

Sudden cardiac death

Patients who died from cardiac disease no later than 24 hours after the onset of the acute symptoms were included

in this group. The relation of the symptoms to heart disease was based on the case history, possible electrocardiographic changes, possible rises in enzyme values and autopsy findings. The next-of-kin, the physician or ambulance staff were contacted in all cases of death in order to determine the mode as well as the time of death in relation to the onset of symptoms. Patients resuscitated after clinical cardiac arrest were also included in the group of sudden cardiac death provided the duration of their symptoms did not exceed 24 hours.

Electrocardiographic changes

The electrocardiograms were evaluated using the definitions of Goldman (1976).

Ventricular ectopic beats

Ventricular ectopic beats were characterized by a premature QRS complex of abnormal morphology without a preceeding P wave. The QRS complexes of the ventricular type had differing appearances in the same lead in cases of multiform ventricular ectopic beats. The term R on T phenomenon was used for ventricular ectopic beats with an $R-R'/QT$ ratio of less than 1.0. Ventricular tachycardia was defined as at least three consecutive ventricular ectopic beats with a frequency of 100/min or more.

Ventricular fibrillation was defined as rapid, irregular oscillations of varying magnitude, form and duration. In addition, the ventricular ectopic beats were graded quantitatively, using a modified Lown & Wolf (1971) scale: Grade 1: no ventricular ectopic beats, Grade 2: few, uniform ventricular ectopic beats, Grade 3: frequent, uniform ventricular ectopic beats, i.e. more than 1/min or 30/hour at any time, Grade 4: multiform ventricular ectopic beats, Grade 5: paired ventricular ectopic beats, Grade 6: R on T phenomenon, Grade 7: ventricular tachycardia and Grade 8: ventricular fibrillation.

The term complicated ventricular arrhythmia was used in the following for the occurrence of multiform and paired ectopic beats, R on T phenomenon or ventricular tachycardia (Lown Grades 4-7). Uniform ventricular ectopic beats were termed uncomplicated ventricular arrhythmias irrespective of their number (Lown Grades 2-3).

ST segment displacement

The displacement was measured 60 msec after the J point. A ST depression of at least 0.1 mV with a flat or downward sloping contour was required in order to classify the depression as significant.

Risk factors

Hypercholesterolaemia was defined as a se-cholesterol greater

than 8.2 mmol/l measured after at least 6 hours of fasting and after the acute phase.

Hypertension was present in patients on antihypertensive treatment at the time of admission or when the patient had a diastolic blood pressure of more than 100 mm Hg following repeated measurements.

Patients under antidiabetic treatment on admission or with a fasting plasma glucose higher than 8.4 mmol/l and/or an abnormal glucose tolerance test after the acute phase were considered as suffering from diabetes mellitus.

Obesity was defined as at least 10% over-weight in relation to normal, as stated by Natvig (1975).

Smokers were considered as patients who later than three months prior to admission had smoked at least one cigarette or one cigar or a corresponding amount of pipe tobacco daily (World Health Organization 1971).

Cardiac history

Congestive heart failure prior to admission was considered as being present provided the condition had been diagnosed during a previous hospital admission or the patient was under treatment for such a condition.

During their stay in the coronary care unit the patients were divided into four classes, as suggested by Killip & Kimball (1967). The New York Heart Association classification (1964) into four groups was used in connection with the follow-up examinations.

Cardiomegaly was evaluated employing the X-ray of the chest taken during maximum inspiration, usually in the standing position. The thoracic width was measured at the height of the diaphragmatic cupola, while the heart width was measured as the sum of the maximum deviation of the heart shadow from the midline to each side. A cardio-thoracic ratio was calculated.

Data registration

All collected data were successively registered on special forms by the author. From these they were transferred to machine punch cards with the co-operation of the data-processing department of the hospital.

Some data were also recorded on a magnetic tape by means of a Hewlett-Packard 9810A desk computer connected to a Hewlett-Packard 9865 Casette Memory.

Data processing

The punch cards were processed by an IBM System 370/138 programmed in Fortran IV. Some of the data were processed further by means of a Hewlett-Packard 9810 A desk computer, as required connected to a Hewlett-Packard 9865A Casette Memory and a Hewlett-Packard 9862 X-Y plotter.

Statistical methods

The following statistical methods were used:

Student's t-test for means of two samples.

Linear coefficient of correlation.

Chi squared contingency table.

Fisher's exact test.

Mann-Whitney rank sum test for unpaired data.

Provided a difference is stated as significant without a P value being given then $P < 0.05$.

DISCUSSION

The inclusion criteria were preferred in order to obtain an unselected group of patients with myocardial infarction. An upper age limit of 70 years was used due to the necessity of co-operation from the patient with the ambulatory monitoring. Other investigations employing electrocardiographic tape recordings have used an upper age limit of 65 years (Moss et al. 1971, Rehnqvist 1976) or 70 years (Åbjörn et al. 1977, Federman et al. 1978), while others again include older patients (Van Durme 1975, Vismara et al. 1975, de Soyza et al. 1978). An upper age limit is in all probability expedient in order to avoid too many drop-outs and large numbers of poor quality tapes when outpatients are studied.

The choice of a follow-up period of six months with regard to the repeated monitoring has been based on a desire to examine patients in the period where the myocardium is presumed to be most electrically unstable (Lown et al. 1975), and where the mortality is high (Hofvendahl 1971, Thygesen et al. 1974). Provided the investigation permits an iden-

tification of patients with a high risk of sudden cardiac death, then it is essential that this can take place during the late hospital or early post-hospital phase if prophylactic measures are to have any quantitative effect.

The analysis of the tapes was carried out employing the computerized electrocardiographic analysis. The stated accuracy of the analysis of ventricular arrhythmias is in agreement with the work of Neilson (1974) using the same arrhythmia computer, and with the work of Harrison et al. (1976) in which a computer system developed at Stanford University was employed.

The automatic analysis was difficult and unsatisfactory in approximately 12% of the recordings, mainly due to intermittent changes in the amplitude and morphology of the QRS complexes, or owing to the presence of high T waves, and less frequently due to electrode errors or functional disturbances in the tape recorder. In the first mentioned cases it can be difficult to adjust the computer so that the number of both false positive and false negative ventricular ectopic beats is acceptable. On the other hand, it is often possible to obtain an acceptable number of false negatives although there will be many false positives. However, the later can be identified on the oscilloscope or by means of the print-out. The monitoring was repeated in cases of obvious technical errors.

In earlier investigations dealing with the same problems as those in the present study, monitoring times of six hours (Moss et al. 1971, Rehnqvist 1976), eight hours (Van Durme 1975), ten hours (Vismara et al. 1975) and in the latest published works of 24 hours (Schulze et al. 1977, Federman et al. 1978) have been employed. It is stated in a publication of Lopes et al. (1975) that approximately 85% of all significant arrhythmias will be observed during 12 hours of monitoring during the day time, while later investigations have demonstrated that the considerable hour to hour and day to day variation makes 24 hours the shortest reliable period of monitoring, especially for quantitative evaluation (Morganroth et al. 1978, Winkle 1978, Møller et al. 1980a). It has been demonstrated in a recent study by Kennedy et al. (1978), that during 48 hours of monitoring of 39 patients with a previous myocardial infarction, the maximum Lown grading occurred after six hours in approximately 65% and after 24 hours in approximately 80% of the patients, while the corresponding figures for the maximum frequency/hour were approximately 30% and 70%. Thus a monitoring period of 24 hours seems to be a reasonable compromise.

An additional object of the present investigation has been to study the diurnal variation in the pattern of ventricular arrhythmias, and to evaluate the difference between the periods of day and night in order to obtain possible

information of prognostic importance and in order to contribute to a more reliable basis for the evaluation of the effect of antiarrhythmic drugs. Thus the results of the analysis of each tape was given for six-hour periods.

The grading of Lown & Wolff (1971) employed in the present investigation has been the object of criticism by Bigger et al. (1977a) in respect of three points in particular: 1) the grading is a mixture of quantitative and qualitative parametres, 2) the quantitative criterion includes maximum and not average values for the number of ventricular ectopic beats and 3) the various types of ventricular arrhythmias were given a priori different prognostic values. The grading of Lown & Wolff has been used in present investigation in order to make the study comparable with others, but at the same time the different types of ventricular ectopic beats have been described individually.

Some metodological and clinical aspects of ambulatory electrocardiographic monitoring have been the object of recent surveys (DeBusk 1975, Gofman 1975, Harrison et al. 1976, Johansson 1977).

SUMMARY

The investigation includes 100 consecutive patients below the age of 70 years, discharged alive after admission for definite acute myocardial infarction.

The patients were primarily admitted to the coronary care unit and connected to the electrocardiographic, non-computerized monitoring system. The treatment was that usually employed in the department. One of the last days prior to discharge, as well as approximately one, three and six months after the infarction each patient was subjected to a 60 second resting electrocardiogram (12 leads) as well as 24-hour electrocardiographic tape-recording (2 leads). A follow-up examination was carried out 12 months and on average 18 months (range 15-22 months) after the infarction.

The 24-hour electrocardiographic monitoring was carried out by means of a small portable tape-recorder with the patient fully mobilized during the first, and as an out-patient during the last three examinations. The tape recording was analyzed at 60 times real time by an arrhythmia computer, the reproducibility and accuracy of which was studied with regard to the detection of ventricular arrhythmias. The 24 hours of recording were divided into 6-hour periods, and the average heart rate calculated and the individual types of ventricular ectopic beats described both quantitatively and qualitatively for each period. In addition, the ventricular arrhythmias were graded as suggested by Lown & Wolf (1971). The occurrence of

a number of other arrhythmias was evaluated for each 24-hour period.

All the data collected were registered on special forms and transferred to punch cards for data processing. The chapter also contains the definitions employed.

CHAPTER III : PATIENTS

The first 100 patients complying with the selection criteria and discharged after the 1st of January 1978 were included.

Practically all patients with acute myocardial infarction from an area with approximately 200.000 inhabitants are admitted to the department and the annual number of patients with acute myocardial infarction is approximately 500.

The 100 patients entered the investigation during the period 2nd January to 2nd August 1978. During this period three patients did not wish to participate, two were resident outside the county of Funen, three were employed by or closely connected to the hospital authorities, while one suffered from catatonic schizophrenia.

The average age of the patients was 58.9 years; 60.2 years (range 44 - 69) for the 20 women and 58.6 years (range 39 - 69) for the 80 men. The age distribution between men and

women in the individual five year groups was not significantly different.

The occurrence of risk factors, presence of heart disease and drug intake prior to the infarction are shown in table 1. Hypertension and obesity were relatively more frequent in the women than in men, but the distribution of the risk factors was not significantly different between the two sexes.

The presence of an earlier myocardial infarction has in most cases been documented from hospital records containing enzyme determinations and electrocardiographic recordings. With regard to angina pectoris, the symptoms within the last 24 hours prior to the development of the acute myocardial infarction have not been included in the classification.

The drug intake prior to the infarction is also shown in table 1. In a number of cases some of the drugs listed were given for conditions other than those associated with heart disease, i.e. diuretics and beta-blocking agents for the treatment of hypertension. There was no significant difference with regard to drug intake between men and women.

The myocardial infarction took place prior to admission in 95 of the 100 patients. In 12 the onset of symptoms was more than 24 hours prior to admission. In five the myocardial infarction occurred in the coronary care unit. Table 2 shows the localization and type of the infarction.

Table 1

Risk factors, previous medical history and drug treatment of 100 patients with acute myocardial infarction.

Clinical data	Females (n=20)	Males (n=80)
Risk factors		
hypercholesterolaemia	2	0
hypertension	7	20
diabetes mellitus	4	10
obesity	12	22
smoking	13	48
Heart disease		
previous infarction	4	18
stable angina	6	24
unstable angina	8	15
heart failure	4	15
Drug treatment		
none	8	51
digitalis	3	8
diuretics	6	24
nitroglycerine	3	13
beta-blocking agents	5	14
verapamil	0	1
quinidine	0	0
procainamide	0	0

Table 2

The acute phase of 100 patients with acute myocardial infarction.

Clinical data	No. of patients
Localization of infarction	
anterior	44
inferior	34
multiple	15
indefinite	7
Type of infarction	
transmural	68
subendocardial	21
uncertain	11
Heart failure	
none	29
mild	57
severe	12
shock	2
Other complications	
clinical cardiac arrest	14

Table 3 shows a number of electrocardiographic findings during monitoring while admitted to the coronary care unit. The heading atrial fibrillation includes patients with both intermittent and permanent atrial fibrillation. Individual patients may be listed in several places. The duration of monitoring varied between one and 25 days, with an average of 6.4 days. Table 4 shows the occurrence of ventricular arrhythmias during the acute illness, prior to the 24-hour electrocardiographic tape recording. It should be emphasized here that monitoring in the coronary care unit was not carried out by means of an arrhythmia computer, but was based partly on the alarm system, triggered when the heart rate became lower or exceeded preset limits, and partly on arrhythmia identification carried out by the cardiac nurses, who kept the oscilloscopes under observation. The electrocardiograms were continuously recorded on tape (Lyrec), so that any desired sequence could be analyzed several times and eventually recorded on paper (Mingo-graph 81, Elema-Schönander).

Table 3

The occurrence of supraventricular arrhythmias and conduction disturbances during the acute phase of myocardial infarction in 100 patients.

Electrocardiographic features	No. of patients
Sinus bradycardia < 50/min	27
Atrial fibrillation	22
Supraventricular tachycardia	15
S-A block grade II	5
S-A block grade III	4
A-V block Mobitz type 1	6
A-V block Mobitz type 2	5
A-V block grade III	5
Asystolia > 5 sec	3
RBBB	7
LBBB	2
LAH	4
LPH	2
RBBB + LAH	1
RBBB + LPH	2

Table 4

Ventricular arrhythmias in the acute phase of the myocardial infarction in 100 patients. Each patient is classed only with the highest grade observed.

Maximum Low grade	No. of patients
1. no VEB	20
2. infrequent VEB	23
3. frequent VEB	10
4. multiform VEB	5
5. paired VEB	9
6. R on T phenomenon	2
7. ventricular tachycardia	19
8. ventricular fibrillation	12

DISCUSSION

The composition of the material is marked first and foremost by the upper age limit of 70 years, this producing an under-representation of women in relation to the infarction population as a whole. Women constitute 24 - 42% in Danish surveys (Christiansen et al. 1971, Møller & Thygesen 1976, Fabriçius-Bjerre et al. 1979, Kjølner et al. 1979), while studies of the arrhythmia pattern in postmyocardial infarction patients with electrocardiographic tape-recording include 13 - 22% women (Van Durme 1975, Vismara et al. 1975, Rehnqvist 1976, Åbjörn et al. 1977), depending on the selection criteria. The occurrence of anterior and inferior infarction in the present material corresponds to that found in Danish investigations (Christiansen et al. 1971, Lyager Nielsen 1973) and in other studies using electrocardiographic tape-recording (Van Durme 1975, Vismara et al. 1975, Rehnqvist 1976, Moss et al. 1977, Schulze et al. 1977, Åbjörn et al. 1977, Federman et al. 1978). Fifty-nine per cent of the infarctions in the investigation of Schulze et al. (1977) were transmural, while Rehnqvist (1976) and Van Durme (1975) found 77% and 96%, respectively.

The occurrence of supraventricular arrhythmias and conduction disturbances are similar to the figures given in an extensive survey of previous studies published by Bigger et al. (1977). The stated incidence of ventricular

arrhythmias during the acute phase of admission must be evaluated on the basis of the fact that 12 patients had had symptoms for more than 24 hours prior to admission, and that the monitoring was carried out without the use of an arrhythmia computer, which is superior to manual surveillance (Romhilt et al. 1973, Vetter & Julian 1975). It has been stated that ventricular arrhythmias occur in all patients when careful continuous electrocardiographic analysis is employed and the patient admitted to hospital within a few hours of the onset of symptoms (Mogensen 1970, Romhilt et al. 1973, Vetter & Julian 1975). The fact that 80% of the patients in the present investigation developed ventricular arrhythmias (95% confidence limits: 71 - 87%) might be an expression of an acceptable monitoring technique.

The patients studied here are, when the age limit is taken into consideration, probably representative of infarction populations as a whole.

SUMMARY

One hundred patients complying with the selection criteria entered the investigation between January the 2nd and August the 2nd 1978. The average age was 60.2 years for the 20 women and 58.6 years for the 80 men. Twenty-two patients had suffered a myocardial infarction, 53 had had angina pectoris and 19 heart failure prior to admission. The localization of the infarction was anterior in 44%, inferior in 34%, anterior + inferior in 15% and uncertain in 7%. Q waves developed as a sign of transmural infarction in 68%. Seventy-one patients had signs of congestive heart failure in the coronary care unit, where the occurrence of supraventricular arrhythmias and conduction disturbances were of the same magnitude as mentioned in a recent survey. In the coronary care unit ventricular arrhythmias occurred in 80% of the patients; ventricular tachycardia was observed in 19% and ventricular fibrillation in 12%.

It is concluded that due to the use of an upper age limit women are under-represented in this study, but that the patients examined were otherwise representative of a Danish infarction population as a whole.

CHAPTER IV : VENTRICULAR ARRHYTHMIAS IN THE FIRST SIX MONTHS AFTER AN ACUTE MYOCARDIAL INFARCTION

Continuous electrocardiographic monitoring has demonstrated ventricular ectopic beats in practically all patients admitted to hospital within the first few hours of the onset of a myocardial infarction (Mogensen 1970, Romhilt et al. 1973). Information during the late hospital phase regarding ventricular arrhythmias has mainly been based on the recording of resting electrocardiograms and exercise tracings (Ericsson et al. 1973, Ibsen et al. 1975).

The introduction of a monitoring technique based on small portable tape recorders has permitted the recording of electrocardiograms over a period of hours in patients carrying out their normal physical activity. Several authors using this technique combined with various types of arrhythmia analysis have studied the occurrence of

arrhythmias during the late hospital phase (Moss et al. 1971, Moss et al. 1975, Van Durme 1975, Vismara et al. 1975, Rehnqvist 1976, Schulze et al. 1977, Federman et al. 1978) and a few of them have repeated the examination after discharge (Van Durme 1975, Moss et al. 1977, Rehnqvist & Sjögren 1977, Federman et al. 1978).

The present investigation was planned with the object of obtaining a qualitative and quantitative evaluation of ventricular arrhythmias in connection with repeated ambulatory monitoring of 24 hours duration, as arrhythmias previously have mainly been studied employing a few hours of monitoring during day light hours only, without the use of an arrhythmia computer.

RESULTS

The time and duration of monitoring

Each of the 100 patients was examined on four occasions during the first six months after the infarction. Four patients died during the period from discharge to the first post-hospital examination, and one patient died in the period between the second and third post-hospital monitoring. One patient moved to another part of the country and could not participate in the final examination. Thus a total of 386 tape-recordings were actually carried out. Table 5 shows the time intervals from infarction to monitoring, as well as the duration of the tape-recordings.

Table 5

Time and duration of 24-hour electrocardiographic tape-recording performed on 100 postmyocardial infarction patients.

n=number of tape recordings.

	Periods of time	
	Days from AMI (mean $\pm$ SD)	Minutes of monitoring (mean $\pm$ SD)
Late hospital phase (n=100)	11 $\pm$ 5	1397 $\pm$ 97
First ambulatory control (n=96)	49 $\pm$ 10	1368 $\pm$ 107
Second ambulatory control (n=96)	107 $\pm$ 16	1345 $\pm$ 147
Third ambulatory control (n=94)	189 $\pm$ 14	1337 $\pm$ 159

Medicamental treatment

Table 6 shows the medicamental treatment at the time of examination. An increasing number of patients were under treatment with digoxin due to heart failure, while diuretics were employed on a decreasing number of patients. Verapamil and beta-blocking agents were most often used for angina pectoris, and less frequently as anti-arrhythmics. The medicamental treatment in relation to the occurrence of arrhythmias is dealt with later in this chapter.

Resting electrocardiogram

Table 7 shows the findings during a 60 second resting electrocardiogram recorded immediately prior to the start of each tape-recording. The average heart rate was not significantly different during the four recordings. One patient had atrial fibrillation throughout the whole period of investigation. Forty-eight of the patients had ventricular ectopic beats on the resting electrocardiogram, of these nine patients on two and five patients on three recordings. During the four examinations, ventricular ectopic beats were found in 12%, 15%, 24% and 19% of the resting electrocardiograms, respectively. Ventricular ectopic beats thus occurred significantly more frequently during the second post-hospital recording than during the late hospital phase and the first post-hospital examination ($P < 0.05$). At the third ambulatory control, complicated ventricular ectopic beats only occurred in a single patient. ST-ele-

Table 6

Drug treatment during electrocardiographic tape-recording performed during the late hospital phase and the posthospital period in 100 patients with myocardial infarction. Some patients were treated with more than one drug mentioned.

n=number of tape-recordings.

	Time of monitoring			
	LHP (n = 100)	FAC (n = 96)	SAC (n = 96)	TAC (n = 94)
Digoxin	25	28	29	36
Diuretics	65	55	46	43
Beta-blockers	15	18	17	16
Verapamil	1	1	2	6
Nitroglycerine	-	17	20	16
Quinidine	9	7	8	7
Procainamide	1	1	1	0

Table 7

Electrocardiographic findings during a 60 second resting electrocardiogram.
n=number of recordings.

Parametre	Time of ECG-recording			
	LHP (n = 100)	FAC (n = 96)	SAC (n = 96)	TAC (n = 94)
Heart rate (min^{-1})				
mean	75	76	75	76
SD	14	15	14	14
range	50-115	52-118	44-110	47-118
Sinus rhythm	99	95	95	93
Atrial fibrillation	1	1	1	1
RBBB	4	3	3	3
LBBB	1	0	0	0
LAH	9	8	10	8
RBBB+LAH	3	2	2	2
S-A block, grade II or III	0	0	0	0
A-V block, grade I	1	2	1	1
A-V block, grade II or III	0	0	0	0
SVEB present	1	6	2	5
VEB present	12	14	23	18
bigeminy	2	2	5	0
multiform	1	2	1	0
paired	1	1	0	1
RonT	0	0	0	0
VT	0	0	0	0
ST-elevation > 1 mm	42	27	19	22
ST-depression > 1 mm	13	7	2	6

Table 8

Electrocardiographic findings during 24-hour electrocardiographic tape-recording performed four times within the first six months after an acute myocardial infarction.

n=number of tapes.

Parametre	Time of monitoring			
	LHP (n = 100)	FAC (n = 96)	SAC (n = 96)	TAC (n = 94)
Sinus rhythm	99	95	95	93
Atrial fibrill. (persistent)	1	1	1	1
Atrial fibrill. (intermitt.)	0	2	1	1
Sinus bradycardia < 50/min *	15	13	14	9
Sinus tachycardia >150/min *	3	11	8	1
SVEB present	83	93	94	86
SVT	4	2	1	1
A-V block, Mobitz type 1	0	0	0	0
A-V block, Mobitz type 2	2	2	0	0
A-V block, grade III	1	0	0	0
S-A block, grade II	2	2	1	7
S-A block, grade III	0	0	0	0

* Mean value of at least 3 R-R intervals

vation of more than one mm was significantly more frequent during the late hospital phase than at the controls at three and six months ($P < 0.01$).

24-hour electrocardiographic monitoring

Table 8 summarizes a number of findings during the electrocardiographic tape-recording. Sinustachycardia occurred in particular in connection with the first and second ambulatory control. Supraventricular ectopic beats were common, but no attempt was made to quantitate this type of arrhythmia.

The occurrence of ventricular arrhythmias is depicted in figure 5, and together with the average heart rate described in more detail in table 9. The average heart rate remained constant throughout the first six months after the infarction, and at the same level as the heart rate of the resting electrocardiogram. A comparison of the average heart rate on the resting electrocardiograms and that of the tape-recordings showed a linear correlation with a coefficient of correlation of 0.75 or more. An example of this is shown in figure 6.

The number of ventricular ectopic beats was calculated both as the average number per hour of monitoring as well as the average number per 10,000 QRS complexes. The values showed a very large dispersion and no normal distribution. The number of ventricular ectopic beats calculated in both ways

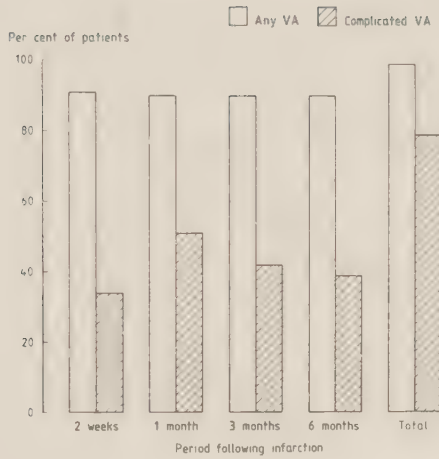
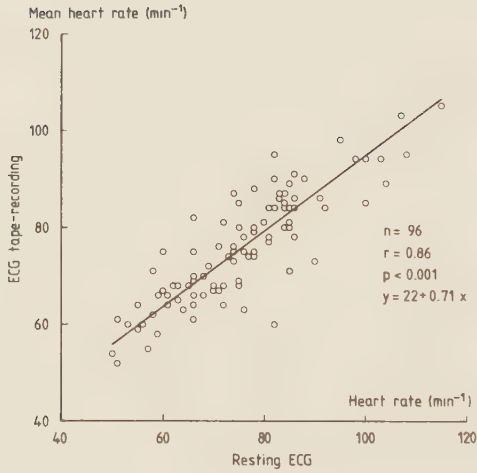


Figure 5

The occurrence of ventricular arrhythmias (VA) during 24-hour electrocardiographic tape-recording.



Figur 6

Correlation between heart rate on resting electrocardiogram and during 24-hour ambulatory electrocardiographic monitoring one month after infarction.

n = number of patients.

Table 9

Heart rate and ventricular ectopic beats during 24-hour electrocardiographic tape-recording performed four times within the first six months after an acute myocardial infarction. Each patient is classed only with the highest Lown grade observed. n = number of tapes.

Parametre	Time of monitoring			
	LHP	FAC	SAC	TAC
	(n = 100)	(n = 96)	(n = 96)	(n = 94)
Mean heart rate (min^{-1})				
mean	76	77	76	77
SD	11	12	11	11
range	52-105	55-106	48-110	52-103
Mean VEB (hour^{-1})				
median	1.1	3.1	3.4	2.8
range	0-273	0-912	0-324	0-559
Mean VEB ($10,000 \text{ QRS}^{-1}$)				
median	2.1	6.6	7.1	4.3
range	0-433	0-1808	0-668	0-419
Highest Lown grade				
1. no VEB	9	10	10	9
2. infrequent VEB	38	21	33	31
3. frequent VEB	19	16	14	17
4. multiform VEB	15	25	19	13
5. paired VEB	14	12	14	16
6. RonT	2	4	1	1
7. VT	3	8	5	7

were significantly higher during the first and second ambulatory monitorings than during the late hospital phase ($P < 0.05$). The number of patients with complicated ventricular arrhythmias was highest in connection with the first ambulatory examination, namely 51% of the patients against 34%, 41% and 39% of the patients at the other monitorings. The occurrence at the first ambulatory monitoring was significantly more frequent than during the late hospital phase ($P < 0.05$). Table 10 shows a more detailed picture of the ventricular arrhythmias during monitoring, and confirms the progression from late hospital phase to the first posthospital monitoring. With regard to the four monitorings as a whole, ventricular ectopic beats occurred in 98% of the patients, multiform in 70%, paired in 47%, R on T phenomenon in 9% and ventricular tachycardia in 19% (not shown in the tables). If the types of arrhythmias are considered in the 94 patients who completed all four monitorings, two had no ventricular ectopic beats at any time, 19 only uniform ectopic beats while six patients had complicated ectopic beats in all four monitorings.

Quantitative contra qualitative arrhythmia pattern

Table 11 demonstrates a clear relationship between the number of ventricular ectopic beats and the various types of ventricular arrhythmias. On the other hand a large number of ventricular ectopic beats are not necessarily accompanied by complicated forms of arrhythmias, inasmuch

Table 10

Ventricular arrhythmias during 24-hour electrocardiographic tape-recording performed four times within the first six months after an acute myocardial infarction. n=number of tape-recordings.

	Time of monitoring				Significance	
	LHP (n=100)	FAC (n=96)	SAC (n=96)	TAC (n=94)	All groups [*]	LHP/FAC ^{**}
Any VEB	91	86	86	85	NS	NS
bigeminy	14	30	32	25	< 0.01	< 0.01
multiform	23	45	32	26	< 0.01	< 0.01
paired	15	16	14	19	NS	NS
RonT	3	5	1	1	NS	NS
VT	3	8	5	7	NS	NS
Mean VEB (hour ⁻¹)						
> 1	51	55	64	58	NS	NS
> 5	30	46	44	38	< 0.05	< 0.05
> 10	19	37	33	32	< 0.05	< 0.01
> 60	4	9	11	7	NS	NS
Mean VEB (10,000 QRS ⁻¹)						
> 1	58	71	72	62	< 0.05	< 0.05
> 5	38	50	54	47	NS	< 0.05
> 10	30	41	44	36	NS	NS
> 60	7	19	19	15	< 0.01	< 0.05

* Chi squared test

** Fisher's exact test

Table 11

The occurrence of various qualitative types of ventricular ectopic beats in relation to the number of ventricular ectopic beats during the same tape-recording.

n=number of tape-recordings.

Ventricular ectopic activity	Mean VEB/10,000 QRS			
	< 1 (n = 85)	1-9 (n = 112)	10-99 (n = 111)	≥ 100 (n = 40)
Bigeminy	2 (2%)	18 (16%)	51 (46%)	30 (75%)
Multiform	10 (12%)	35 (31%)	64 (58%)	17 (43%)
Paired	1 (1%)	8 (7%)	32 (29%)	23 (58%)
RonT	0 (0%)	0 (0%)	6 (5%)	4 (10%)
VT	0 (0%)	6 (5%)	9 (8%)	8 (20%)
None of these	73 (86%)	60 (54%)	26 (23%)	6 (15%)

as 15% of the patients with more than 100 ventricular ectopic beats per 10.000 QRS complexes - corresponding to more than approximately 1000 ventricular ectopic beats per day - had no complicated types of arrhythmias including bigeminy.

Comparison of arrhythmias in the Coronary Care Unit and during tape-recording

Table 12 shows the occurrence of complicated ventricular ectopic beats in the coronary care unit in relation to the four monitorings. It may be seen that the increased occurrence of complicated ventricular arrhythmias during the first ambulatory control results, in the great majority, from a progression in the pattern of arrhythmias in patients with complicated ventricular arrhythmias in the coronary care unit.

Comparison between ventricular arrhythmias on the resting electrocardiogram and during 24-hour tape-recording

Table 13 shows the occurrence of ventricular arrhythmias during tape-recording following a resting electrocardiogram with or without ventricular ectopic beats. Ventricular ectopic beats on the resting electrocardiogram were, with the exception of R on T phenomena, connected with significantly increased occurrence of ventricular arrhythmias during the tape-recording with regard to both quantity and quality.

Multiform and paired ventricular ectopic beats occurred

Table 12

Number of patients showing no or uncomplicated ventricular arrhythmias (UVA) or complicated ventricular arrhythmias (CVA) during 24-hour electrocardiographic tape-recording in relation to ventricular arrhythmias as in coronary care unit.

Ventricular arrhythmias in coronary care unit	Ventricular arrhythmias during 24-hour tape-recording							
	Late hospital phase		First ambulatory control		Second ambulatory control		Third ambulatory control	
	UVA	CVA	UVA	CVA	UVA	CVA	UVA	CVA
No or uncomplicated	36	17	30	22	37	15	33	19
Complicated	30	17	17	27	20	24	24	18

Table 13

The occurrence of ventricular ectopic beats during 24-hour electrocardiographic tape-recording in relation to the occurrence of ventricular ectopic beats on the 60 second resting electrocardiogram recorded immediately prior to the start of each tape-recording.
n=number of related registrations.

24-hour electrocardiographic tape-recording	Ventricular ectopic beats on 60 seconds resting electrocardiogram		p-value
	Present (n = 67)	Absent (n = 319)	
VEB present	67 (100%)	281 (88%)	< 0.005
bigeminy	35 (52%)	66 (21%)	< 0.01
multiform	32 (48%)	94 (29%)	< 0.005
paired	29 (43%)	35 (11%)	< 0.001
RonT	3 (4%)	7 (2%)	NS
VT	8 (12%)	15 (5%)	< 0.05
Mean VEB/10.000 QRS > 10	56 (84%)	95 (30%)	< 0.001
Mean VEB/10.000 QRS > 60	33 (49%)	27 (8%)	< 0.001

on four and three resting electrocardiograms, respectively. The following tape-recording showed multiform ventricular ectopic beats in six, paired ventricular ectopic beats in six and ventricular tachycardia in two of these patients. An average of more than ten ventricular ectopic beats per 10.000 QRS complexes occurred on six of the seven tapes.

Ventricular ectopic beats occurred on only one third (10/31) of the resting electrocardiograms registered immediately prior to a tape-recording showing R on T phenomenon or ventricular tachycardia.

In 52 patients ventricular ectopic beats did not occur on any of the resting electrocardiograms. Thirty-two (62%) of these patients had complicated ventricular ectopic beats on at least one tape-recording, seven (13%) had ventricular tachycardia.

Ventricular arrhythmias during 24-hour electrocardiographic tape-recording in relation to medicamental treatment

Table 14 shows the occurrence of complicated ventricular arrhythmias in relation to the drug therapy at the time of the four monitorings. Taking the recordings as a whole, 54 tapes were recorded during treatment with digoxin and antiarrhythmics (beta-blockers, verapamil, quinidine, procainamide), 54 with antiarrhythmics alone, 64 with digoxin alone, while neither digoxin nor antiarrhythmics were given during the recording of 214 tapes. As can be seen from table 6 beta-blockers were the drug with antiarrhythmic

Table 14

Number of tapes with complicated ventricular arrhythmias during 24-hour electrocardiographic tape-recording in relation to medicament treatment. Antiarrhythmics include beta-blockers, verapamil, quinidine and procainamide. n=total number of tapes during each monitoring.

	Drug treatment				Significance
	+ digoxin + antiarr- hythmica	- digoxin + antiarr- hythmica	+ digoxin - antiarr- hythmica	- digoxin - antiarr- hythmica	
Late hospital phase (n=100)	6 (67%)	5 (29%)	7 (44%)	16 (28%)	NS
First ambulatory control (n=96)	7 (47%)	4 (36%)	6 (46%)	32 (56%)	NS
Second ambulatory control (n=96)	5 (33%)	7 (54%)	6 (43%)	21 (39%)	NS
Third ambulatory control (n=94)	6 (40%)	7 (52%)	11 (52%)	13 (29%)	NS
All four monitorings (n=386)	24 (44%)	23 (43%)	30 (47%)	82 (38%)	NS

effect most frequently used.

Table 14 demonstrates no clear relationship between treatment and the arrhythmias, and if the monitorings are considered as a whole (lowest line in the table) no significant difference was observed between the occurrence of complicated arrhythmias in the four treatment groups. It may be seen from table 15 that patients under antiarrhythmic treatment had a significantly slower heart rate than the other patients ($P < 0.01$). Evaluated quantitatively, the patients under treatment with digoxin without simultaneous antiarrhythmic treatment had a considerably greater number of ventricular ectopic beats than the other patients ($P < 0.01$). There was only a significant difference between the groups with regard to the occurrence of ventricular ectopic beats as bigeminy and no definite pattern could be discerned.

DISCUSSION

The late hospital phase

The occurrence of ventricular ectopic beats during the late hospital phase of an acute myocardial infarction varies from investigation to investigation, as can be seen in table 16. The reason for this must be differences in the populations studied, the duration of monitoring, the spontaneous variation in ventricular ectopic activity, and the electrocardiographic analysis.

Table 15

Heart rate and ventricular arrhythmias during electrocardiographic tape-recording in relation to medicamental treatment. Data from the four monitorings are pooled. Antiarrhythmics include beta-blockers, verapamil, quinidine, procainamide.

n=number of tape-recordings.

	Drug treatment			
	+ digoxin	+ digoxin	- digoxin	- digoxin
	+ antiarrhythmica (n=54)	- antiarrhythmica (n=64)	+ antiarrhythmica (n=54)	- antiarrhythmica (n=214)
Mean heart rate (min^{-1})				
mean	71	81	70	78
SD	11	12	10	12
Mean VEB (hour^{-1})				
median	1.7	11	2.8	0.8
range	0-136	0-559	0-324	0-912
Mean VEB (10.000 QRS^{-1})				
median	5.0	32	6.7	2.1
range	0-307	0-1410	0-1411	0-1808
Bigeminy	17 (31%)	27 (47%)	13 (24%)	44 (21%)
Multiform	20 (37%)	22 (34%)	17 (25%)	67 (31%)
Paired	11 (20%)	19 (30%)	6 (11%)	36 (17%)
RonT	2 (4%)	1 (2%)	2 (4%)	5 (2%)
VT	2 (4%)	5 (8%)	3 (6%)	13 (6%)

With regard to the composition of the materials it would appear that those mentioned were unselected patient groups, even though exclusion criteria are not stated in detail in several of the investigations (Moss et al. 1975, Vismara et al. 1975, Schulze et al. 1977), and 31% of the patients in the study of Federman et al. (1978) were excluded for various reasons. In the last mentioned investigation the patients participated in a randomized study with beta-blockers. The age criteria can also be of importance, as ventricular ectopic beats in patients with ischaemic heart disease have been found to increase with age (Hinkle et al. 1969, Ruberman et al. 1977). However, a factor of greater importance is undoubtedly the duration of monitoring and the spontaneous day to day variation as earlier mentioned.

The analytical procedure in the studies quoted, were mainly manual without the use of arrhythmia computers (Moss et al. 1975, Van Durme 1975, Vismara et al. 1975, Schulze et al. 1977), while a commercial arrhythmia computer was used part of the time in one of the studies (Federman et al. 1978). The manual procedure consisted of observation of the electrocardiogram on an oscilloscope during play-back, normally at 60 times the recording speed. These analyses were eventually supplemented by measurement of the RR-interval and quantitation of the number of QRS complexes. The reliability of such a method has not been reported. In the paper of Rehnqvist (1976) telemetry was employed and the whole electrocardiogram written out on paper using a paper

Table 16

Ventricular arrhythmias in the late hospital phase of an acute myocardial infarction.
A comparison with previous studies.

	Moss et al. 1975	Van Durme 1975	Vismara et al. 1975	Rehnqvist 1976	Schulze et al. 1977	Federman et al. 1978	Present study
Number of patients	193	150	64	100	81	95	100
Age (years)	< 66	27-81	39-84	44-65	mean 57	37-68	39-69
Hours of registration	6	8	8	6	24	24	24
Criterion of frequent VEB	> 20/h	> 1/min.	-	> 5/min.	> 30/h	-	-
Per cent with							
any VEB	51	59	77	70	65	77	91
frequent VEB	7	43	-	10	5	-	-
multiform VEB	9	24	-	22	19	-	23
paired VEB	3	14	-	11	-	-	14
RonT	20	2	-	2	1	-	3
VT	-	5	8	1	-	-	3

speed of 10 mm/sec. It has thus been possible in that work to carry out a more exact quantitation of the occurrence of ventricular arrhythmias.

The occurrence of ventricular ectopic beats is higher in the study presented here than in any of the others. This is undoubtedly a result of the long period of monitoring and the use of an arrhythmia computer. The general impression is, even with such short periods of monitoring as six to eight hours, that between one half and three quarters of the patients have ventricular ectopic beats.

A number of problems occurred, when comparing the various types of ventricular arrhythmias, due to differences in the definitions, especially with regard to the term "frequent" ventricular ectopic beats. In the study of Moss et al. (1975) the number of ventricular ectopic beats was quantitated despite a manual analytical technique, and the values stated were therefore average figures, as in the study of Rehnqvist (1976), for the whole period of monitoring. In the other investigations the criterion "frequent" was used provided this occurred at least once during the monitoring period. If the present study is compared to the findings of Moss et al. (1975), 13% of the patients will comply with the criterion of an average of more than 20 ventricular ectopic beats per hour. The criterion of Van Durme (1975) regarding at least one episode with more than one ventricular ectopic beat per minute will have been complied with by the great majority of the 43% of the patients

with complicated ventricular ectopic beats. A direct comparison with the work of Rehnqvist (1976) is impossible. In the work of Schulze et al. (1977) each patient is tabulated under the presumed most malignant form according to the grading of Lown & Wolf (1971), which as noted by Bigger et al. (1977a), would indicate an apriori prognostic evaluation.

The occurrence of multiform and paired ventricular ectopic beats is fairly uniform with the exception of the study of Moss et al. (1975). The remarkably high incidence of R on T phenomenon in the latter investigation in all probability depends on a definition of R on T as $RR'/QT < 1.10$ as compared to < 1.0 in the other studies. The occurrence of ventricular tachycardia, defined as at least three consecutive ventricular ectopic beats, has also been fairly constant from study to study. It is not possible to state, with regard to the works of Vismara et al. (1975) and Federman et al. (1978), the occurrence of the various types of ventricular ectopic beats, but in the former study frequent, multiform and paired ventricular ectopic beats or R on T phenomenon occurred in 41% of the patients, and in the latter, these ventricular ectopic beats or ventricular tachycardia occurred in 42% of the patients.

During exercise testing performed about two weeks after an infarction ventricular ectopic beats were noted in 19% to 42% of the patients (Ericsson et al. 1973, Ibsen et al. 1975, Åbjörn et al. 1977) and are thus considerably more

infrequent than during tape-recording of even 6-8 hours duration. Multiform ventricular ectopic beats were observed in 8-16% of the patients (Ericsson et al. 1973, Åbjörn et al. 1977) and ventricular tachycardia in 0.5 - 3%. The last mentioned percentage was based on the occurrence of ventricular tachycardia in a single patient of 31 in the investigation of Åbjörn et al. (1977).

The post hospital phase

Data from studies applying electrocardiographic tape-recording to myocardial infarction patients during the posthospital phase are summarized in table 17, and the results of the present investigation added for comparison. In only four of the investigations were the patients studied during both the late hospital phase and the posthospital period (Van Durme 1975, Moss et al. 1977, Rehnqvist & Sjögren 1977, Federman et al. 1978). In the study of Van Durme (1975) eight hours of monitoring were carried out during day light hours each month during the first year after the infarction, while Moss et al. (1975) followed up the patients using six hours of monitoring five months after the infarction. Rehnqvist & Sjögren (1977) carried out six hours of telemetry - divided between three hours at night and three during the day - one year after the infarction and Federman et al. (1978) 24 hours of monitoring each three months for the first year after the infarction. The results stated by Moss et al. (1975) and Rehnqvist & Sjögren (1977) are entirely confined to findings during the posthospital monitoring, while those of

Table 17

Ventricular arrhythmias in the posthospital period of a myocardial infarction.
A comparison with previous studies.

	Kotler et al. 1973	Van Durme * 1975	Moss et al. 1977	Rehnqvist & Sjögren 1977	Ruberman et al. 1977	Federman et al.* 1978	Vorpahl et al. 1978	Present study*
Duration and number of registrations.	12 h x ?	8 h x 11	6 h x 1	6 h x 1	1 h x 1	24 h x 5	24 h x 1	24 h x 4
No. of patients	160	150	231	122	1739	74	55	100
Age (years)	30-64	27-81	66	44-65	35-74	37-68	mean 52	39-69
Time post-infarction	> 3 m	0-12 m	5 m	12 m	> 3 m	0-12 m	6-12 m	0-6 m
Criterion of frequent VEB	> 1/min	> 1/min	> 20/h	-	>10/h	> 1/10 QRS	> 2/min	> 1/min
Per cent with								
any VEB	80	75	63	78	51	80	89	98
frequent VEB	18	57	17	-	26	45	15	89
multiform VEB	18	35	18	30	†	39	27	70
paired VEB	20	24	11	11	†	26	26	47
RonT	-	6	16	0	26	4	-	9
VT	3	15	1	6	†	1	13	19

* including data from the late hospital phase

Van Durme (1975), Federman et al. (1978) and of the present study are a summation of the occurrence of arrhythmias during all monitorings. Thus these latter studies include approximately 100 hours of monitoring of the individual patient. This factor is of vital importance with regard to the evaluation of the frequencies, but factors such as different monitoring periods within the day, and within the posthospital period must be presumed to play a role. In addition to this, the patients of Federman et al. (1978) as earlier mentioned took part in a pharmacological study, and 34 of the initial 108 patients did not complete the investigation, of these only four due to death.

A comparison of ventricular arrhythmias in these three studies employing a total monitoring period of approximately 100 hours shows the highest incidence of all types in the present investigation. With regard to ventricular tachycardia, this can partly be explained by the difference in definitions, as Federman et al. (1978) used at least four consecutive ectopic beats. No direct comparison is possible with regard to the frequency criteria. As previously mentioned, Van Durme (1975) employed a manual analytical technique and Federman et al. (1978) primarily a manual technique then later computerized analysis. Finally it must be mentioned that the two studies in contrast to the present included the period from six to twelve months after the infarction, where the occurrence of ventricular arrhythmias was found to be slightly decreasing.

A few authors have been concerned with the course of ventricular arrhythmias during the months after an infarction. In the work of Moss et al. (1977) where eight hours of monitoring were performed in the late hospital phase as well as five months later in 231 postinfarctional patients, all types of ventricular ectopic beats except ventricular tachycardia were more frequent at the follow-up. A corresponding tendency can be found in the present work with comparison of the patterns during the late hospital phase and that six months after infarction. Twenty-four patients changed from uncomplicated to complicated ventricular arrhythmias, 18 patients *vica versa* following comparison of the above mentioned two monitoring periods. In agreement with the present study, but in contrast to Van Durme (1975), the work of Federman et al. (1978) demonstrates a progression in the ventricular ectopic pattern shortly after discharge. The reason for this progression must possibly be ascribed to the increased physical and mental stress, which occurs when the more protective hospital environment is left. However, it is rather perplexing that the increased stress does not produce a rise in the average heart rate, although this does not necessarily mean that the heart rate did not fluctuate more than during hospitalization. A comparison of the results for the period 0-6 months with the period 7-12 months after the infarction shows a decrease in ventricular ectopic beats both from a quantitative and qualitative point of view in the work of Van Durme (1975),

while Federman et al. (1978) found no obvious difference. Rehnqvist & Sjögren (1977) found a significant progression from the late hospital phase to telemetry carried out one year later, which is possibly a result of a progression taking place shortly after discharge.

Comparison of ventricular ectopic beats in the Coronary Care Unit and during electrocardiographic tape-recording

Following a comparison of the occurrence of complicated ventricular ectopic beats in the coronary care unit (46%) and during the tape-recording in the late hospital phase (34%), the present investigation similar to that of de Soyza et al. (1978) (71% versus 50%) shows a decrease in contrast to Vismara et al. (1975a) (29% versus 41%). These studies are not directly comparable, but it is curious that the increase was observed in the study employing the shortest period of tape-recording. The present investigation demonstrates that the increase in the number of patients with complicated ventricular ectopic beats occurring shortly after discharge results from the fact that patients with complicated ventricular arrhythmias in the coronary care unit and uncomplicated ventricular arrhythmias during the late hospital phase develop complicated ventricular ectopic beats again during the posthospital monitoring. This means that the pattern of arrhythmias in the coronary care unit are, to a certain extent, predictive with regard to the arrhythmias following discharge. It should in this connection be mentioned that patients with

ventricular tachycardia or fibrillation in the coronary care unit are more prone to the development of ventricular tachycardia during the subsequent tape-recordings than other patients (Møller et al. 1980). Finally it should be noted that in the work of de Soyza et al. (1978) patients with paroxysmal ventricular tachycardia during the acute phase had complicated ventricular ectopic beats during 24-hours of tape-recording significantly more frequently than other patients, when the recording was carried out on average 19 months after the infarction.

Comparison of resting electrocardiogram and 24-hour electrocardiographic tape-recording for the demonstration of ventricular ectopic beats

The investigation shows that 1) the occurrence of any ventricular ectopic beats on the resting electrocardiogram is related to both qualitative and quantitative high occurrence during tape-recording, 2) the occurrence of multiform or paired types on the resting electrocardiogram suggest the presence of advanced types of ventricular arrhythmias during tape-recording and 3) two thirds of the patients with serial recordings of resting electrocardiograms without ventricular ectopic beats have complicated forms during tape-recording.

These findings are hardly surprising when it is taken into consideration that a 24-hour electrocardiographic recording is 1440 times longer than a 60 second resting electrocardiogram and at the same time includes periods of both phy-

sical and mental stress. Thus Moss et al. (1971) found that of 101 postinfarctional patients studied during the late hospital phase, six had ventricular ectopic beats on the resting electrocardiogram against 72 during six hours of tape-recording, and Vismara et al. (1977) that of 101 patients with stable ischaemic heart disease, 50% had complicated ventricular arrhythmias during 10 hours of tape-recording against 19% showing ventricular ectopic beats on at least one of four resting electrocardiograms recorded during the first four weeks after the tape-recording.

The insensitivity of the resting electrocardiogram even with serial recordings has been confirmed by Federman et al. (1978) who found complicated ventricular ectopic beats in 43% of the patients with four resting electrocardiograms recorded during the first year after the infarction showing no ventricular ectopic beats. Similarly, Vismara et al. (1977) found complicated ectopic beats during ten hours of tape-recording in 33% of 53 patients with an average of 10 resting electrocardiograms without ventricular ectopic beats recorded during a follow-up period of two years.

Comparison of ventricular ectopic beats on the exercise electrocardiogram and during 24-hour tape-recording

The present investigation does not include an evaluation of ventricular arrhythmias during exercise testing as compared to electrocardiographic tape-recording. In the hospi-

tal phase of myocardial infarction such a comparison has only been carried out in a single study (Åbjörn et al. 1977) which showed the greatest frequency of ventricular arrhythmias during exercise testing and concluded that this method was superior to 24-hour tape-recording. Several comparative studies are available in respect of patients with ischaemic heart disease, of which the earliest (Kosowsky et al. 1971, Crawford et al. 1975) considered exercise testing as the better of the two methods. The latest investigations, carried out with improved monitoring and analytical techniques (Ryan et al. 1975, De Backer et al. 1977, Boudoulas et al. 1978, Poblete et al. 1978, Vorpahl & Blümchen 1978, Møller & Thayssen 1980) suggest that tape-recording is the more sensitive method of the two, particularly with regard to the occurrence of complicated ventricular arrhythmias, but the two methods appear to supplement each other. Whether or not ventricular arrhythmias detected by means of the two methods are of different prognostic value has not been the object of study.

Medicamental therapy

The investigation was not designed to provide an evaluation of the effect of individual antiarrhythmic drugs. The patients were treated, as mentioned earlier, using the normal procedure of the department, and without knowing the results of the tape-recordings. It should in this connection be mentioned that the patients in the work of Van Durme (1975) had their drug therapy discontinued during monito-

ring, while this was not the case in the other studies quoted. As in other investigations (Rehnqvist 1976, Federman et al. 1978) no pronounced relationship could be observed between the occurrence of ventricular arrhythmias and the medicamental treatment.

There is no possibility of knowing what the pattern of arrhythmias would have been like without the drug therapy but in any case the therapy was definitely unable to eliminate even complicated ventricular arrhythmias.

SUMMARY

Ventricular ectopic beats were found in approximately 90% of the patients at each of the four tape-recordings. Complicated ventricular arrhythmias occurred in 34%, 51%, 41% and 39% of the patients at the four occasions, and were thus significantly more frequent during the first posthospital monitoring as compared to the late hospital phase ($P < 0.05$). This progression in the pattern of arrhythmias mainly includes patients, who had had complicated ventricular ectopic beats in the coronary care unit.

For the four monitorings as a whole, ventricular ectopic beats occurred in 98% of the patients, multiform in 70%, paired in 47%, R on T phenomenon in 9% and ventricular tachycardia in 19%. A close correlation was found between the number of ventricular ectopic beats and the different types of ventricular arrhythmias, even though a large number of the ventricular ectopic beats on a minority of tapes was not associated with the occurrence of complicated ventricular ectopic beats.

Ventricular ectopic beats were present on 67 resting electrocardiograms from 48 patients and were combined with a significantly increased occurrence of all types of ventricular ectopic beats, apart from R on T, in the immediately following tape-recording. Ventricular ectopic beats occurred on only one third of the resting electrocardiograms recorded prior to a monitoring showing R on T or ventricular tachycardia.

It is concluded that ventricular ectopic beats occur in practically all postinfarctional patients and in the majority as complicated forms. The number of patients with complicated forms increases significantly in connection with discharge and is fairly constant throughout the following six months.

Thus an antiarrhythmic therapy may at least cover this period.

CHAPTER V : DIURNAL VARIATION IN HEART RATE AND VENTRICULAR ECTOPIC ACTIVITY

Both bradycardia (Han et al. 1966, Chadda et al. 1974) and tachycardia (Chadda et al. 1974) have been found in animal experiments to increase the occurrence of ventricular arrhythmias. As both of these conditions are governed by the tone of the autonome nervous system, it would be logical to expect an effect of the latter on the incidence of ventricular arrhythmias. A number of aspects concerning both the sympathetic and parasympathetic component have recently been discussed in extensive surveys (Lown et al. 1977, Corr & Gillis 1978).

It is difficult, in patients with a myocardial infarction, to evaluate the degree of sympathetic and parasympathetic tone of the heart, and in clinical studies it will normally be necessary to employ the heart rate as an indicator of tone. In the prehospital phase of myocardial infarction considerable disturbances have been observed in the cardiac autonomic tone in the form of a

pronounced tendency to both bradycardia and tachycardia (Webb et al. 1972), but the precise frequency at which autonomic disturbances precipitate ventricular arrhythmias is uncertain (Geddes 1978). In the coronary care unit it does not appear that the heart rate during sinus rhythm (Norris et al. 1972) nor the circulating catecholamines (Videbaek et al. 1972) are of any real importance with regard to the occurrence of ventricular arrhythmias.

The heart rate is successively reduced during sleep and reaches its lowest value after about six hours (Tzivoni & Stern 1973). The fall in heart rate results from an increase in parasympathetic and a corresponding decrease in sympathetic activity (Tzivoni & Stern 1973, Pickering et al. 1977). However, other factors must be of importance, inasmuch as heart transplant patients - with a totally denervated heart - also show considerable diurnal variation (Winkle, personal communication 1979).

It has been found in different groups of patients by means of electrocardiographic tape-recording, that the number of ventricular ectopic beats is frequently reduced during sleep (Lown et al. 1973, Winkle et al. 1975, Pickering et al. 1977), and that this reduction is better correlated to heart rate than to the level of sleep, as evaluated electroencephalographically (Pickering et al. 1978).

In order to make a contribution to the elucidation of some of these problems, one of the objects of the present study, has been to evaluate the diurnal variation in heart rate and ventricular ectopic beats.

RESULTS

As mentioned earlier, the day was divided into four 6-hour periods commencing at midnight. Table 18 shows the duration of monitoring during these time intervals. The monitoring was usually started and terminated during the period 6-12 a.m.. Table 19 provides details of the diurnal variation in heart rate. In all four monitorings the mean heart rate was significantly slower at night (0-6 a.m.) as compared to the remainder of the day ($P < 0.01$). No significant difference was found from monitoring to monitoring.

Figure 7 shows the occurrence of both "any" and complicated ventricular ectopic beats during the four monitoring periods and table 20 provides more detail. There was little variation within the four monitorings with regard to "any" ventricular ectopic beats, and no significant difference was observed when comparing the same 6-hour period from monitoring to monitoring. The occurrence of complicated ventricular arrhythmias showed no diurnal variation in the late hospital phase and six months after the infarction. A more pronounced (insignificant) diurnal variation could be seen at the monitoring after one and three months, with the lowest fre-

Table 18

Duration in minutes (mean $\pm$ SD) of electrocardiographic tape-recording for each 6-hour period of the day.

n=number of tapes.

	Period			
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.
Late hospital phase (n=100)	356 $\pm$ 30	336 $\pm$ 50	344 $\pm$ 35	360 $\pm$ 0
First ambulatory control (n=96)	352 $\pm$ 40	301 $\pm$ 71	356 $\pm$ 13	359 $\pm$ 3
Second ambulatory control (n=96)	355 $\pm$ 26	292 $\pm$ 75	354 $\pm$ 27	356 $\pm$ 26
Third ambulatory control (n=94)	355 $\pm$ 28	281 $\pm$ 84	356 $\pm$ 21	355 $\pm$ 23

Table 19

Diurnal variation of mean heart rate per minute.

n=number of tapes.

	Period			
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.
Late hospital phase				
n	100	99	100	100
mean	69	78	79	76
SD	11	12	12	13
range	49-97	56-109	59-115	57-105
First ambulatory control				
n	95	96	96	96
mean	68	81	83	77
SD	11	14	13	13
range	49-95	50-125	56-125	51-120
Second ambulatory control				
n	92	96	96	96
mean	67	80	82	75
SD	11	14	13	12
range	46-105	49-109	50-117	48-112
Third ambulatory control				
n	91	94	94	94
mean	67	80	83	77
SD	10	13	13	11
range	46-90	55-109	55-128	48-112

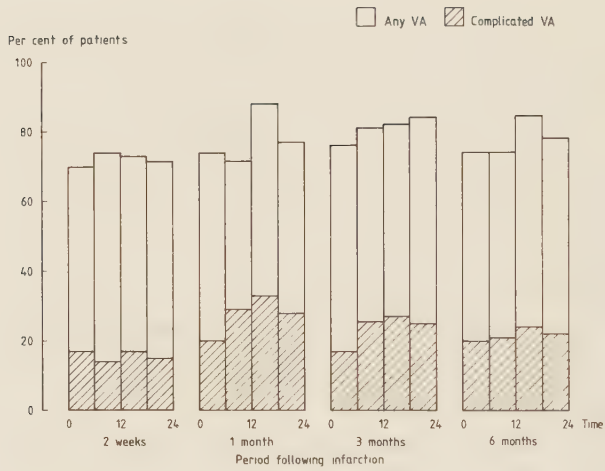


Figure 7

Diurnal variation of ventricular arrhythmias (VA) during 24-hour electrocardiographic tape-recording. Each day is divided into four 6-hour periods.

Table 20

Diurnal variation in the pattern of ventricular arrhythmias as evaluated qualitatively. Figures are given as number of tapes.

Ventricular arrhythmias	Period				Significance *	
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.	All groups	Night/ day **
Late hospital phase						
None	30	26	27	29		
Uncomplicated	53	59	56	56	NS	NS
Complicated	17	14	17	15		
First ambulatory control						
None	25	28	16	23		
Uncomplicated	50	39	47	45	NS	NS
Complicated	20	29	33	28		
Second ambulatory control						
None	24	19	18	16		
Uncomplicated	51	51	51	55	NS	NS
Complicated	17	26	27	25		
Third ambulatory control						
None	26	26	18	22		
Uncomplicated	45	47	52	50	NS	NS
Complicated	20	21	24	22		

* Chi squared contingency table (3x4 and 3x2)

** Night = 0-6 a.m., day = 6.a.m. - 12 p.m.

quency from midnight to 6 a.m.. During the day-time complicated arrhythmias were significantly more frequent one month after the infarction than during the late hospital phase ($P < 0.05$); no difference was found between the night periods.

Tables 21 and 22 deal with the quantitative aspects. When using the Mann-Whitney test, it was found with regard to the three posthospital monitorings, that there was a higher average number of ventricular ectopic beats per hour in the period 6 a.m. to 12 p.m. than at night ($P < 0.05$), while the number of ectopic beats expressed in relation to the number of QRS complexes (corrected for heart rate) did not differ in the two periods. The occurrence of various types of ventricular ectopic beats can be seen from table 23. No significant variation was found within the day, even though the period 12-6 p.m. had, on the whole, the highest frequency. No significant difference was observed when comparing night and day.

From table 24 it can be seen that the most rapid average heart rate and the highest average number of ventricular ectopic beats per hour occurred most frequently (insignificantly) in the period 12-6 p.m.. Further, the lower part of the table shows that the number of ventricular ectopic beats was more evenly distributed throughout the 24 hours after correction for differences in heart rate. These data, together with those previously presented in this chapter, suggest a definite relationship between heart rate

Table 21

Diurnal variation of the average number of ventricular ectopic beats per hour.

The number of tapes during each period can be seen from table 19.

Mean VEB (hour ⁻¹)	Period			
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.
Late hospital phase				
median	0.3	0.7	0.7	0.5
range	0-588	0-297	0-351	0-284
First ambulatory control				
median	1.8	2.7	2.9	2.8
range	0-1021	0-751	0-1020	0-853
Second ambulatory control				
median	1.8	3.7	3.3	4.9
range	0-314	0-292	0-530	0-444
Third ambulatory control				
median	1.5	3.2	2.5	1.6
range	0-137	0-1696	0-699	0-285

Table 22

Diurnal variation of the average number of ventricular ectopic beats per 10.000 QRS complexes.

The number of tapes during each period can be seen from table 19.

Mean VEB (10.000 QRS ⁻¹)	Period			
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.
Late hospital phase				
median	1.0	1.6	1.7	1.3
range	0-1012	0-452	0-610	0-504
First ambulatory control				
median	4.5	5.1	5.8	5.0
range	0-2363	0-1455	0-1828	0-1734
Second ambulatory control				
median	4.8	6.9	7.2	10.0
range	0-716	0-614	0-1015	0-902
Third ambulatory control				
median	3.7	5.4	5.1	3.7
range	0-350	0-3981	0-1640	0-350

Table 23

Diurnal variation in the occurrence of different types of ventricular ectopic beats. Figures are given of number of tapes showing each type. The total number of tapes during each period can be seen from table 19.

Ventricular arrhythmias	Period			
	0-6 a.m.	6-12 a.m.	12-6 p.m.	6-12 p.m.
Late hospital phase				
Bigeminy	8	9	8	7
Multiform	10	13	10	9
Paired	6	5	9	5
RonT	0	1	1	1
VT	1	2	0	0
First ambulatory control				
Bigeminy	15	21	21	21
Multiform	20	27	31	27
Paired	7	10	14	9
RonT	2	4	2	0
VT	1	4	3	2
Second ambulatory control				
Bigeminy	13	19	23	23
Multiform	16	20	23	23
Paired	4	9	10	8
RonT	0	1	1	1
VT	0	4	2	1
Third ambulatory control				
Bigeminy	10	11	17	12
Multiform	16	16	19	16
Paired	9	11	11	4
RonT	0	1	0	1
VT	0	4	2	4

and ventricular ectopic activity.

In order to study this phenomenon more thoroughly all the tapes with a reasonably high number of ventricular ectopic beats permitting statistical analysis (600 per day or more) were selected. Sixty-five tapes complied with this criterion. The average number of ventricular ectopic beats was calculated for both day (6 a.m. - 12 p.m.) and night (0-6 a.m.). Figure 8 shows the percentage change when day was compared to night. Calculated per hour (left column), 16 (25%) tapes showed an increase in ectopic activity at night, 28 (43%) tapes a reduction of at least 75%. After correction for heart rate (right column), the majority of tapes still showed a reduction in ectopic frequency during the night. This indicates a decrease in the night hours considerably greater than the corresponding decrease in heart rate itself. Digoxin and antiarrhythmics were given during only five of the 28 tapes with a reduction of ectopic activity of 75% or more. Table 25 demonstrates that patients with a large reduction in ectopic activity (corrected for heart rate) at night may be characterized, in particular, by a slow night heart rate - presumably indicating a weak sympathetic tone. A comparison between day and night with regard to the qualitative pattern of arrhythmias showed unchanged complicated types in 31 tapes, unchanged uncomplicated types in 10 and a shift from complicated to uncomplicated in 24. Thus no qualitative progression occurred at night, even in tapes with an increasing

Table 24

The number of patients with the highest average heart rate and average number of ventricular ectopic beats in each 6-hour period. Some patients may appear in more than one period.

Values = 0 are excluded.

n=number of tape-recordings

Parametre	Number of patients				
	LHP (n=100)	FAC (n=96)	SAC (n=96)	TAC (n=94)	TOTAL (n=386)
Maximum mean heart rate (min^{-1})					
0-6 a.m.	1	1	1	1	4
6-12 a.m.	43	35	43	38	159
12-6 p.m.	52	55	50	52	209
6-12 p.m.	22	18	12	13	65
Maximum mean VEB (hour^{-1})					
0-6 a.m.	23	14	13	14	64
6-12 a.m.	23	18	26	26	93
12-6 p.m.	34	38	23	34	129
6-12 p.m.	32	22	26	16	96
Maximum mean VEB ($10,000 \text{ QRS}^{-1}$)					
0-6 a.m.	26	18	15	17	76
6-12 a.m.	19	16	25	24	84
12-6 p.m.	27	34	19	26	106
6-12 p.m.	20	20	27	18	85

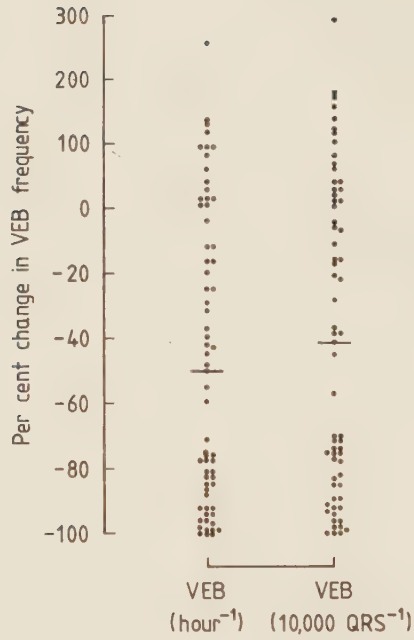


Figure 8

The percentage change in ventricular ectopic beats from day to night (0-6 a.m.) calculated per hour (left column) and per 10,000 QRS complexes (right column). Median value indicated by cross bar. n=65.

Table 25

The change in the average number of ventricular ectopic beats per 10,000 QRS complexes from day to night as related to average heart rate within each period.

n=number of tapes.

Change in the average number of VEB from daytime to night	Mean heart rate per min ($\pm$ SD)	
	Daytime (6 a.m. - 12 p.m.)	Night (0 - 6 a.m.)
Increase (n=16)	83 $\pm$ 10	77 $\pm$ 11
Reduction 1-75% (n=21)	82 $\pm$ 15	71 $\pm$ 12
Reduction 76-100% (n=28)	79 $\pm$ 9	65 $\pm$ 10

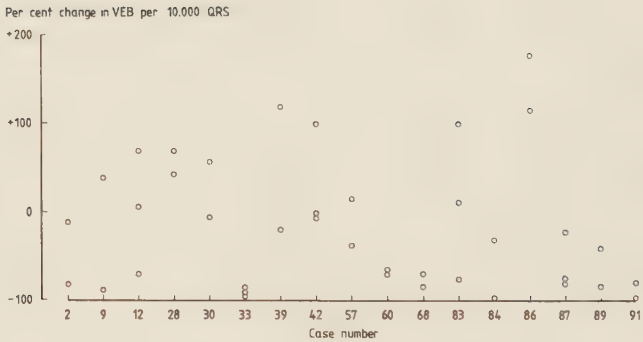


Figure 9

Percentage change when comparing the average number of ventricular ectopic beats per 10,000 QRS complexes during the day (6 a.m. - 12 p.m.) with the average number during the night (0-6 a.m.). Each circle represents a tape-recording.

ectopic activity.

In order to evaluate the reproducibility of the diurnal pattern in the individual patient, tapes from 17 patients with more than one tape containing at least 600 ectopic beats per day were employed. Figure 9 shows the change from day to night for each individual tape, and it can be seen that the changes were quite often different from tape to tape in the same patient. Medicamental treatment had no influence on this.

DISCUSSION

The present study shows that the occurrence of "any" ventricular ectopic beats is almost constant throughout the day. Complicated ventricular arrhythmias showed no significant diurnal variation, even though there was a tendency to a higher incidence during the period 12-6 p.m., a time at which the majority of patients also had the highest frequency of ventricular ectopic beats and the highest mean heart rate. Corresponding studies have not been reported in postmyocardial infarction patients, but in a work of Rehnqvist & Sjögren (1977) it is stated that the presence of ventricular arrhythmias during three hours of telemetry performed both during sleep and under physical activity was not significantly different, neither in the late hospital phase nor at the renewed examination one year later.

The amount of information regarding ventricular arrhythmia-

as increases with increasing duration of monitoring (Kennedy et al. 1978) and 24 hours seem to be the shortest reliable period (Winkle 1978, Morganroth et al. 1978, Møller et al. 1980a). However, should it be necessary to employ a shorter period, then it would appear from the present study that it is most expedient to include the hours 12 to 6 p.m..

The relationship between heart rate, as an expression of the tone of the autonome nervous system, and the occurrence of ventricular arrhythmias in connection with an acute myocardial infarction is on number of points controversial. In a study of 72 patients investigated in a mobile coronary care unit less than 30 minutes after the onset of an acute myocardial infarction, signs of sympathetic hyperactivity were observed in 36% and of parasympathetic in 55% (Webb et al. 1972). Both conditions can presumably play a role in the activation of arrhythmias as it has been shown in animal experiments that both abnormally slow rate (Han et al. 1966, Chadda et al. 1974) and tachycardia (Chadda et al. 1974) increase the occurrence of ventricular arrhythmias. In the coronary care unit, Norris et al. (1972) found no relation between the occurrence of sinus bradycardia and ventricular ectopic beats as repetitive or as R on T phenomenon.

In other animal experimental investigations vagus stimulation increased the threshold of electrically induced ventricular fibrillation (Kent et al. 1973), and provided protection against spontaneous, fatal ventricular arrhythmias

during the acute phase of an infarction (Corr & Gillis 1974). This effect was not only dependent on the bradycardia, but also influenced by the magnitude of sympathetic tone on the heart (Lown et al. 1977). Sympathetic hyperactivity increases the occurrence of ventricular arrhythmias (Verrier et al. 1975, Schwartz et al. 1976).

If these latter observations can be related to human myocardial infarction, it must be expected that the number of ventricular ectopic beats will be reduced during sleep, where the heart rate is successively reduced as a result of the shift in autonomic cardiac tone (Tzivoni & Stern 1973, Pickering et al. 1977).

In two earlier publications including patients with ischaemic heart disease and persons without apparent heart disease (Lown et al. 1973) and patients with mitral valve prolapse (Winkle et al. 1975) a reduction in the number of ventricular ectopic beats during sleep was observed by means of 24-hour electrocardiographic tape-recording. As the number of ventricular ectopic beats, however, is expressed per time unit, it is not possible to determine to what extent the reduction follows changes in heart rate. In a work of Pickering et al. (1977) a correlation was found between the fall in heart rate and the reduction in the number of ventricular ectopic beats, particularly in patients with a large reduction in the number of such beats during sleep. The number of ventricular ectopic beats was better correlated to heart rate than to the level of consciousness in a later investigation by Pickering et al. (1978), where

the various phases of sleep were determined in 13 patients by means of continuous registration of an electroencephalogram and eye movements. Others have found an increased occurrence of ventricular ectopic beats during the so-called rapid eye movement (REM) sleep, where the autonomic tone varies considerably (Smith et al. 1972, Rosenblatt et al. 1973).

The present study does not allow of an exact estimation of the period of sleep, although it may be assumed that the majority of patients will be asleep during the hours 0-6 a.m..

The present investigation suggests that the pattern of ventricular arrhythmias with a qualitative evaluation does not show any pronounced variation within the 24 hours. Evaluated quantitatively, the number of ventricular ectopic beats is reduced in the majority of patients at night - presumably secondarily to an increased parasympathetic tone and a reduced sympathetic tone, expressed as a reduction in heart rate. As a large reduction in heart rate to a slow but not abnormal sleeping rate was followed by an even greater reduction in ectopic activity, it is possible that the degree of sympathetic tone plays a more important role than the heart rate itself. Thus it would appear, based on the investigation of Pickering et al. (1978) with propranolol induced sympathetic blockade and vagus mediated bradycardia obtained by phenylephrine, that the tone of the sympathetic nervous system plays a greater role than that of the para-

sympathetic system, as suppression of the number of ventricular ectopic beats with the same reduction of the heart rate was greatest when the latter was produced by the beta-blockade. On the other hand, propranolol may have antiarrhythmic effect via mechanisms other than pure beta-blockade. It has recently been demonstrated by Woosley et al. (1979) that propranolol has a dose dependent antiarrhythmic effect, which continues after the plasma concentration producing full beta-blockade has been achieved.

Medication is unlikely to have been of importance in the present study as beta-blockers were given during only one of the 28 recordings with a large sleep reduction. As digoxin and antiarrhythmics were used only during five of these 28 recordings the patients presumably belonged to the group "least ill". This would explain the assumed weak sympathetic tone.

The association between bradycardia and increased occurrence of ventricular ectopic beats found by Han et al. (1966) and Chadda et al. (1974) may be explained by the pathologically slow rates obtained in these canine experiments possibly causing a reduced cardiac output with a decrease in myocardial perfusion.

The practical aspects of the findings may be a guide to a better selection of the most advantageous antiarrhythmic drug. It seems reasonable that patients with a large reduction in ectopic activity in connection with a reduction in heart rate may benefit from beta-blocker treatment main-

taining the heart rate at lower levels throughout the day. On the other hand, the lack of reproducibility of the diurnal variation in some patients makes the question more complicated.

Patients with a faster heart rate during both the day and night - and often with an increased ectopic activity during the night - are probably the patients with the more advanced myocardial damage. Even though it may be tempting to give beta-blockers to these patients in order to lower the heart rate, this may be inadvisable due to the negative inotropic effect. Therefore the most rational approach is to concentrate on improvement of the left ventricular function and optimal treatment of heart failure.

SUMMARY

The day was divided into four 6-hour periods and the heart rate as well as the pattern of ventricular ectopic beats described for each of these. The occurrence of complicated ventricular ectopic beats as a whole, or as individual types, did not differ significantly within the day, but a tendency was seen to the lowest frequency at 0-6 a.m. and the highest at 12-6 p.m.. Calculated per hour, the average number of ventricular ectopic beats was, during the posthospital monitorings, lower at night (0-6 a.m.) as compared to the rest of the day ($P < 0.05$), but after correction for heart rate, the ectopic activity was not significantly dependent on the time of day. Thus there appears to exist a relationship between heart rate and the number of ventricular ectopic beats. A more thorough examination of all tapes with many ventricular ectopic beats (600 per day or more) showed when comparing day (6 a.m. - 12 p.m.) and night that the number of ventricular ectopic beats per 10,000 QRS complexes increased in 25% of the tapes and was reduced by at least 75% in 43%. The reduction in the number of ventricular ectopic beats was particularly high in those patients with a large reduction in heart rate. The variation in the occurrence of ventricular ectopic beats thus depends on factors other than the heart rate itself, presumably the magnitude of the sympathetic tone and the severity of the underlying heart disease. From a practical point of view, patients with a large reduction in ventricular ectopic activity in connec-

tion with reduction in heart rate may benefit from beta-blocker treatment. Unfortunately the diurnal variation differed considerably from tape to tape in the individual patient, making the selection of a suitable antiarrhythmic drug difficult. A monitoring period shorter than 24 hours is not recommendable, but if necessary the period 12-6 p.m. should be included.

CHAPTER VI : RELATIONSHIP BETWEEN VENTRICULAR ARRHYTHMIAS AND CLINICAL PARAMETRES

The relation between ventricular arrhythmias during long-term monitoring of postmyocardial infarction patients and a number of clinical parametres is still uncertain, as the investigations available on this subject (Moss et al. 1975, Vismara et al. 1975, Schulze et al. 1977, Federman et al. 1978, Rehnqvist 1978, Vorpahl & Blümchen 1978) have, in many respects, provided diverging results. The relationship between the extent of the myocardial injury and ventricular arrhythmias is of particular interest, as studies from recent years indicate that it will be possible to limit the size of an infarction by various forms of intervention during the early phase (Braunwald & Maroko 1976, Gold et al. 1976). Many investigations (Peel et al. 1962, Norris et al. 1970, Sobel et al. 1972, Helmers 1974, Thygesen et al. 1976, Vedin et al. 1977, Geltman et al. 1979, Kjøller et al. 1979) connote that the prognosis during the first years

after infarction depends on factors which must be considered an expression of or dependent on the extent of the myocardial damage. As at the same time certain forms of ventricular arrhythmias in postinfarctional patients in a number of studies have been found to increase the risk of sudden cardiac death during the posthospital phase (Coronary Drug Project Research Group 1973, Kotler et al. 1973, Van Durme 1975, Vismara et al. 1975, Ruberman et al. 1977, Rehnqvist et al. 1978, Moss et al. 1979) one may assume that there exist a relationship between the extent of the myocardial injury and ventricular arrhythmias after discharge.

RESULTS

The average heart rate during monitoring was to a considerable extent independent of a number of clinical parameters. No difference was observed between men and women. Patients younger than 60 years had an insignificantly more rapid heart rate than the others. During the first two monitorings a faster rate was seen in patients with transmural than in those with subendocardial infarctions ($P < 0.01$, < 0.05). The site of the infarction was of no importance. The occurrence of complicated VEB did not differ significantly between recordings with an episode of heart rate $> 150/\text{min}$ (43%), a heart rate $< 50/\text{min}$ (31%) and the others (43%).

Table 26 shows the pattern of ventricular arrhythmias in relation to age, sex, risk factors and cardiac history prior to the admission. It can be seen that the older

Table 26

Relation between age, sex and medical history prior to admission and the occurrence of ventricular arrhythmias during electrocardiographic monitoring. n=number of tapes.

UVA=no or uncomplicated ventricular arrhythmias, CVA=complicated ventricular arrhythmias.

	Late hospital phase		Total posthospital period		Significance	
	UVA (n=66)	CVA (n=34)	UVA (n=161)	CVA (n=125)	Within late hospital phase	Within post-hospital period
Age > 60 years	26	22	68	63	< 0.05	NS
Males	53	27	129	104	NS	NS
Hypertension	19	8	51	30	NS	NS
Diabetes	8	6	17	22	NS	NS
Obesity	22	13	48	49	NS	NS
Smoking	42	19	95	76	NS	NS
Myocardial infarction	12	10	82	70	NS	NS
Angina pectoris	29	24	82	70	< 0.05	NS
Heart failure	4	15	27	23	< 0.001	NS

half of the patients had complicated ventricular arrhythmias more often than the younger patients in the late hospital phase; from this point there was no difference between the two groups. Patients suffering from pre-admission angina pectoris or congestive heart failure had an increased frequency of complicated arrhythmias during the late hospital phase. More than one half of these latter patients (10/19) had previously suffered a myocardial infarction.

Table 27 demonstrates that with regard to ventricular arrhythmias there was no significant difference as to whether the infarction was anterior or inferior. Similarly, patients with transmural infarction did not differ to patients with subendocardial infarction. However, it can also be seen that there was a general tendency to an increased occurrence of all qualitative types of arrhythmias in patients with inferior infarction and a higher incidence of both qualitative and quantitative patterns in patients with transmural infarction.

Of the anterior infarctions 25/44 (57%) were transmural against 26/34 (76%) of the inferior (NS). In cases of transmural infarction, 88% of those with inferior and 80% with anterior localization suffered from complicated arrhythmias during at least one monitoring (NS). Thirty-six percent (16/44) of the anterior infarctions were subendocardial, and in these patients complicated arrhythmias occurred in 9/16 (56%), which is significantly less than with

Table 27

Ventricular arrhythmia during the total period of electrocardiographic tape-recording.
n=number of patients.

Ventricular ectopic beats	Infarct site		Infarct type		Heart failure in CCU	
	Anterior (n=44)	Inferior (n=34)	Transmural (n=68)	Subendocar- dial (n=21)	Present (n=71)	Absent (n=29)
Bigeminy	23 (52%)	25 (74%)	42 (62%)	10 (48%)	47 (66%) *	12 (41%)
Multiform	27 (61%)	27 (79%)	48 (71%)	10 (48%)	50 (70%)	20 (69%)
Pairs	19 (43%)	17 (50%)	28 (41%)	9 (43%)	40 (56%) *	7 (24%)
RonT	3 (7%)	3 (9%)	7 (10%)	0 (0%)	5 (7%)	4 (14%)
Ventricular tachy- cardia	5 (11%)	10 (29%)	17 (25%)	1 (5%)	14 (20%)	5 (17%)
Complicated ven- tricular arrhythmias	31 (70%)	30 (88%)	55 (81%)	13 (62%)	59 (83%)	20 (69%)
Mean VEB >10 per 10.000 QRS complexes	30 (68%)	23 (68%)	49 (72%)	10 (48%)	56 (79%) **	13 (45%)

* $p < 0.05$, ** $p < 0.01$

transmural infarctions either inferior or anterior ($P < 0.05$). The measured maximum lactic dehydrogenase activity in serum did not differ significantly between anterior and inferior transmural infarctions ($P=0.054$), but was significantly greater with transmural anterior as compared to subendocardial anterior infarctions ($P < 0.01$). Thus it would appear that the site of the infarction plays a less important role than the question of transmurality. The latter can, based on enzyme activity, be a result of differences in the extent of the myocardial injury. This would also explain the difference in the occurrence of arrhythmias in patients with and without congestive heart failure in the coronary care unit.

An attempt has been made to determine to what extent the severity of myocardial injury influences the occurrence of ventricular arrhythmias. The following patients were excluded from this part of the investigation: 20 patients with a previous myocardial infarction, 10 who were not admitted to the coronary care unit at the latest 24 hours after the onset of symptoms, as well as two patients complying with both these criteria. A study was made of the remaining 68 patients to determine to what extent the myocardial injury, expressed as the maximum rise in serum creatine kinase activity was of importance in respect of ventricular arrhythmias during the six months of follow-up. Figure 10 shows the average maximum serum creatine kinase activity for patients with complicated ventricular arrhythmias

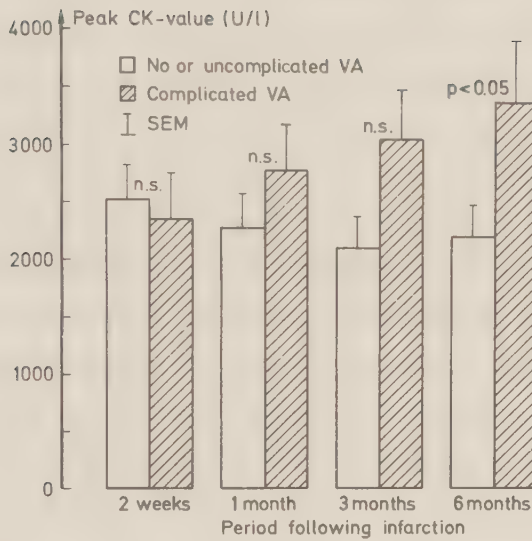


Figure 10

Maximum serum creatine kinase activity (CK) in relation to ventricular arrhythmias during 6 months follow-up.

(n=68 patients)

as compared to the other patients. Patients with complicated ventricular arrhythmias during the three posthospital monitorings had a higher se-creatine kinase activity during admission than the remaining patients; this difference was significant after 6 months ($P < 0.05$). In order to further evaluate the relationship between the number of ventricular ectopic beats and the "size" of the infarction, the patients were divided into a group with small infarctions, characterized by a maximum creatine kinase activity of less than 1500 U/l ($n=29$), and a group with larger infarctions characterized by a maximum creatine kinase activity greater than 1500 U/l ($n=39$). The average number of ventricular ectopic beats per hour did not differ significantly between the two groups during the first three monitorings, while the number of ventricular ectopic beats per hour at the six months monitoring was significantly greater in patients with larger infarctions ($P < 0.05$).

DISCUSSION

The heart rate has not previously been the object of investigation using ambulatory electrocardiographic monitoring of postmyocardial infarction patients. As in persons without apparent heart disease (Clarke et al. 1976), no significant relationship was found between heart rate and age. However, the mentioned study, in contrast to the present, has demonstrated that women without apparent heart

disease have a more rapid heart rate than men. The increased tendency to a slow heart rate in the initial phase of an inferior infarction (Adgey et al. 1971) was not observed during the period of investigation covered by the present study. The significantly more rapid heart rate in cases of transmural as compared to subendocardial infarctions can possibly be explained by more extensive damage to the myocardium with subsequent impairment of pump function in the former cases, so that an increased rate can be a compensatory mechanism to maintain a sufficient cardiac output.

No relationship was demonstrated in this or the investigations of Moss et al. (1975) and Vismara et al. (1975) between sex and ventricular arrhythmias. On the other hand, Van Durme (1975) observed a higher incidence of "any" ventricular ectopic beats and ventricular tachycardia in men during the first year after an infarction. Rehnqvist & Sjögren (1977) more frequently found an unchanged pattern of uncomplicated arrhythmias in women than in men when comparing the late hospital phase with monitoring one year later. There is no obvious explanation of these differences.

The majority of investigators (Moss et al. 1975, Van Durme 1975, Ruberman et al. 1977, Rehnqvist 1978) observed a rising incidence of ventricular arrhythmias with rising age, no doubt due to ischaemic heart disease being a progressive disease.

The presence of heart disease prior to admission was found in the present investigation, as in others (Moss et al. 1975, Rehnqvist 1978), to be of importance with regard to ventricular arrhythmias during the late hospital phase, presumably as these patients had a more severely compromised left ventricular function than other patients (Bleifeld et al. 1977).

If all the myocardial infarction patients were considered together, this investigation confirmed the observation of Federman et al. (1978) of an increased frequency of ventricular arrhythmias in patients with inferior infarction compared to those with anterior localization. While nothing has been mentioned in the above study regarding transmurali-ty, it appears that the explanation in the present study is an over-representation of subendocardial infarctions with anterior localization. The reason being that anterior subendocardial infarctions were found to be related to a significantly lower incidence of ventricular arrhythmias than anterior transmural infarctions, whilst there was no difference between transmural anterior and inferior infarctions. No relationship was found in the majority of other studies between the localization of the infarction and the arrhythmias during the late hospital phase (Schulze et al. 1975, Van Durme et al. 1975, Vismara et al. 1975, Rehnqvist 1978), even though Geltman et al. (1979) state that with small infarctions, a greater number of ventricular ectopic beats occur with inferior than with anterior localization.

The increased occurrence of ventricular arrhythmias in patients with heart failure in the coronary care unit and in patients with transmural as compared to subendocardial infarction can presumably be explained by the fact that these conditions are related to a more extensive myocardial injury with impairment of ventricular performance. Rehnqvist (1978) also found this tendency, whilst Schulze et al. (1975) observed no relationship between the two types of infarction and the pattern of arrhythmias in the late hospital phase. In addition, the latter (Schulze et al. 1978) found no difference between transmural and subendocardial infarctions with regard to the extent of arterial stenosis, left ventricular ejection fraction and wall motion.

A relation has been found during the acute phase of a myocardial infarction between complicated ventricular arrhythmias and the maximum serum activity of the enzyme aspartate-aminotransferase (Mogensen 1970, Chapman 1972). Similarly, a relationship has been observed between infarct size and the number of ventricular ectopic beats (Roberts et al. 1975), as well as the occurrence of ventricular tachycardia during the acute phase (Nordlander & Nyquist 1979). In the last two mentioned investigations, the magnitude of the myocardial infarction was estimated by means of enzyme kinetic models requiring determination of the creatine kinase activity in serum each or every second hour (Shell et al. 1971, Bleifeld et al. 1977). In the present study no such enzyme determinations have been carried out,

and the observed maximum enzyme values have been used as a rough guide of the extent of infarction, as has been found permissible in patho-anatomical studies (Kibe & Nilsson 1967, Erhardt 1974). As a number of patients in the present investigation were admitted more than 24 hours after the onset of symptoms, the maximum value of the enzyme lactic dehydrogenase has initially been employed, as this enzyme is the last to reach maximum levels and maintain these for the longest period (Sobel & Shell 1972). In a sub-group of patients without previous infarctions and admitted to hospital at the latest 24 hours after the onset of symptoms, serum creatine kinase has been employed, as a study from this department has demonstrated a high positive correlation ($r = 0.93$), in patients admitted early, between maximum se-values with the method employed in the present study and peak values found by determination each other hour (Thygesen 1979). The last mentioned peak values were well correlated to the calculated infarction size using Bleifeld's monocompartment model.

No significant relationship was found in the present study or in that of Federman et al. (1978) during the late hospital phase between arrhythmias during 24 hour of monitoring and the "size" of the infarction, while both Schulze et al. (1975) and Rehnqvist (1976) could demonstrate such a relationship. The only investigation including both actual quantitation of the infarct size and 24-hour electrocardiographic monitoring during the posthospital phase of the infarction (Geltman et al. 1979) demonstrated a re-

relationship between the number of ventricular ectopic beats and the size of the infarction. At the same time the investigation showed that the relationship was only significant during monitoring carried out at least six months after the infarction, which is in agreement with the present study. In addition, this study demonstrated a relationship between the "size" of the infarction and arrhythmias, also when the latter are considered from a qualitative point of view. The investigation of Federman et al. (1978) appears to be in close agreement with this.

On the basis of the investigations of others, there is hardly any doubt that the size of the infarction produces its arrhythmia triggering effect via abnormalities of left ventricular wall motion. A high correlation has been demonstrated between infarction size and the ejection fraction in patients with a recent myocardial infarction (Ashburn et al. 1973) and between a low ejection fraction and a high incidence of complicated ventricular arrhythmias in the late hospital phase of a myocardial infarction (Schulze et al. 1975, 1977). During the same phase, a relationship has recently been demonstrated between the degree of coronary artery stenosis and complicated ventricular arrhythmias (Humphries et al. 1978), and the same applies to patients with ischaemic heart disease during the stable phase in the work of Calvert et al. (1977) and Vismara et al. (1977a). while Bethge et al. (1977) also found an association between ejection fraction and the degree of ven-

tricular asynergy but not with the degree of stenosis of the coronary arteries. Based on discriminant analysis, it would appear that the abnormal left ventricular contraction, probably as an expression of myocardial fibrosis, is the decisive arrhythmia associated factor (Sharma et al. 1974, Calif et al. 1978).

SUMMARY

The average heart rate was significantly more rapid with transmural than subendocardial infarctions and insignificantly more rapid in the younger age group. The sex of the patient and localization of the infarction were of no importance.

The occurrence of complicated ventricular arrhythmias during the late hospital phase was significantly associated with a high age as well as the occurrence of angina pectoris and heart failure prior to admission to hospital. These factors played no significant role during the posthospital phase. For the monitorings as a whole, heart failure in the coronary care unit was associated with a significantly and transmural infarction as well as inferior localization with an insignificantly increased occurrence of ventricular arrhythmias, both with regard to quality and quantity. The difference between anterior and inferior infarctions was mainly based on an over-representation of subendocardial infarctions in the former group.

The size of the infarction, expressed by the maximum measured enzyme activity in serum, appears during the first six months after the infarction to play an increasing role with regard to ventricular arrhythmias. After six months both the number of ventricular ectopic beats as well as the incidence of complicated ventricular arrhythmias were significantly greater in patients

with the higher enzyme rises.

It is concluded that the extent of the myocardial injury and the degree of subsequent impairment of left ventricular function are presumably the most important arrhythmia associated factors.

CHAPTER VII : PROGNOSTIC SIGNIFICANCE OF VENTRICULAR ARRHYTHMIAS

The value of the pattern of ventricular arrhythmias as a predictor of sudden cardiac death has become the object of great interest due to a considerable extent to the results of the Tecumseh investigation (Chiang et al. 1969) and to those of the Coronary Drug Project Research Group (1973). Even greater interest has been directed to this subject after it has become possible to carry out long-term ambulatory electrocardiographic monitoring. Several investigators have found, using this method, that certain types of ventricular arrhythmias in patients with ischaemic heart disease are per se a prognostic factor (Ruberman et al. 1977, Rehnqvist 1978, Moss et al. 1979). However, it is still difficult to select well-defined high risk groups. The present investigation is the only one published to date employing repeated 24-hour monitoring combined with computer based electrocardiographic analysis. The possibility of obtaining new prognostic aspects has therefore been

evaluated despite the fact that the total number of patients suffering sudden cardiac death is small.

RESULTS

One case of non-cardiac death (cerebro-vascular stroke), two cases of non-sudden cardiac death and 12 cases of sudden cardiac death occurred (including two cases of cardiac arrest with documented ventricular fibrillation and successful resuscitation) during an average follow-up period of 18 months (range 15-22 months). Nine cases of non-fatal infarction were registered, of these two in patients who later succumbed to sudden cardiac death, and one in a patient with later non-sudden cardiac death. One of the patients with non-sudden cardiac death had a documented re-infarction. Thus twenty of the 100 patients suffered a re-infarction and/or cardiac death.

Sudden cardiac death occurred in five patients within the first six months of the infarction (figure 11), in two patients between six and 12 months and in the last five patients from 12 to 17 months after the initial infarction. The duration of symptoms in seven of the patients was from seconds to a few minutes (cases No. 25,82,58,40,59,49,26) and in three patients (cases No. 84,90,61) approximately two, eight and 10 hours, respectively. Two deaths were unwitnessed: one took place while the person was driving (case 74), the other during sleep (case 75) without the patient attempting to call for help. The first case at least may be presumed to have occurred with a very short duration of symptoms

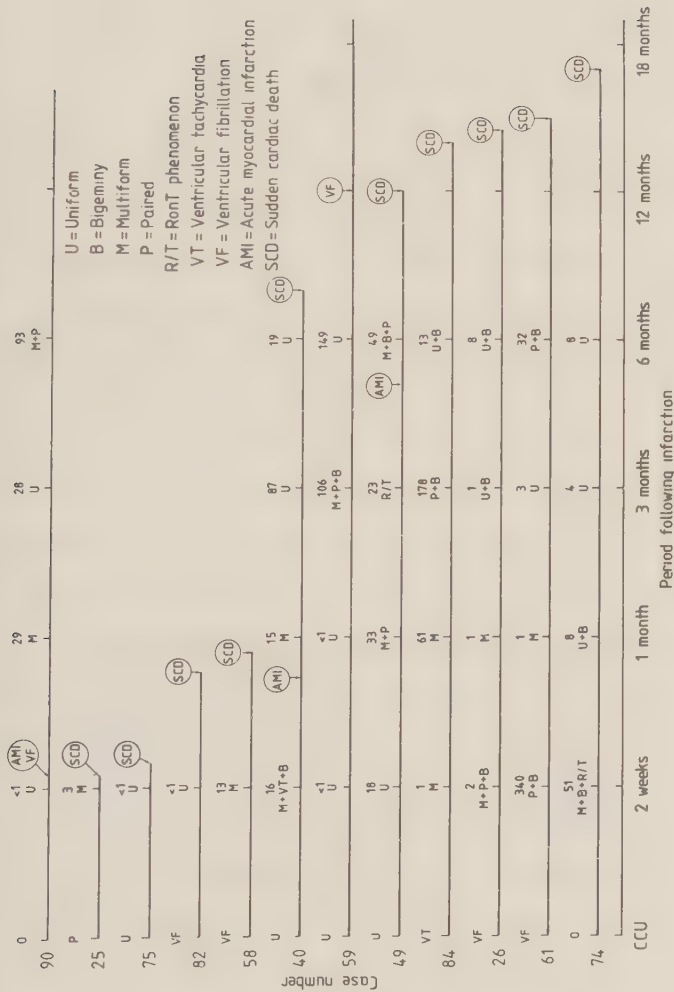


Figure 11

Ventricular arrhythmias during repeated 24-hour electrocardiographic tape-recording in 12 patients suffering sudden cardiac death. The figures give the average number of ventricular ectopic beats per 10,000 QRS complexes within the monitoring in question.

and in the latter case the last contact with the patient was two hours prior to death. Patients No. 90 and 61 had documented re-infarction in connection with the sudden cardiac death. Sudden cardiac death occurred throughout the day. One patient was carrying out heavy physical activity, one drove his car and one slept, while the other patients were at rest, either sitting or lying.

Table 28 and 29 show a comparison between the 12 patients with sudden cardiac death and the 85 patients alive at the time of follow-up. With regard to the parameters employed in table 28, sudden cardiac death was significantly more frequent in patients with a large rise in serum enzyme activity. Further relatively more frequent in connection with multiple localization as well as with the occurrence of congestive heart failure and ventricular tachycardia/fibrillation in the coronary care unit. Table 29 shows the electrocardiographic findings in the late hospital phase. The patients with sudden cardiac death had both on the resting electrocardiogram and the tape-recordings, an insignificantly faster heart rate than the other patients. With regard to ventricular arrhythmias, the majority of qualitative types were more frequent in the group with sudden cardiac death, but the difference was only significant with regard to multiform ventricular ectopic beats ($P < 0.05$). Neither the heart rate nor the pattern of arrhythmia during sleep were of specific prognostic importance.

Table 28

Clinical parameters in relation to sudden cardiac death during an average follow-up period of 18 months (range 15-22 months).

	Patients who died suddenly (n=12)	Patients who survived (n=85)
Age, years		
mean $\pm$ SD	62 $\pm$ 6	58 $\pm$ 8
Males	10 (83%)	67 (79%)
Previous infarction	3 (25%)	19 (22%)
Infarct site		
anterior	5 (42%)	37 (44%)
inferior	2 (17%)	31 (36%)
multiple	4 (33%)	11 (13%)
indefinite	1 (8%)	6 (7%)
Infarct type		
transmural	8 (67%)	57 (67%)
subendocardial	2 (17%)	19 (22%)
uncertain	2 (17%)	9 (11%)
Large infarction (peak LDH > 3000 u/l)	4 (33%)*	8 (9%)
Data from CCU		
Killip class II-IV	10 (83%)	59 (69%)
VT/VF	5 (42%)	25 (29%)

* P < 0.05

Table 29

Electrocardiographic parametres during the late hospital phase
in relation to a sudden cardiac death

	Patients who died suddenly (n=12)	Patients who survived (n=85)
Resting electrocardiogram		
Heart rate (mean $\pm$ SD)	79.9 $\pm$ 12.2	75.0 $\pm$ 14.0
Any VEB	2 (17%)	10 (12%)
Electrocardiographic monitoring (total period)		
Mean heart rate (mean $\pm$ SD)	78.8 $\pm$ 10.0	75.7 $\pm$ 11.6
Any VEB	12 (100%)	77 (91%)
Multiform VEB	6 (50%)*	16 (19%)
Paired VEB	2 (17%)	12 (14%)
RonT VEB	1 (8%)	2 (2%)
Ventricular tachycardia	1 (8%)	1 (1%)
Bigeminy	4 (33%)	9 (11%)
Mean VEB > 1 per 100 QRS	5 (42%)	25 (29%)
Electrocardiographic monitoring (0-6 a.m.)		
Mean heart rate (mean $\pm$ SD)	71.9 $\pm$ 9.0	69.2 $\pm$ 11.5
Any VEB	10 (83%)	58 (68%)
Multiform VEB	3 (35%)	6 (7%)
Paired VEB	0 (0%)	6 (7%)
Mean VEB > 1 per 1000 QRS	2 (17%)	18 (21%)

* P < 0.05

Figure 11 shows the ventricular arrhythmias in the coronary care unit and during the tape-recordings for the 12 patients who succumbed to sudden cardiac death. It can be seen that three cases of sudden cardiac death occurred less than two weeks after a monitoring showing only uniform ventricular ectopic beats (cases No. 90,75,82), and in a further five patients the last monitoring prior to death showed a similar pattern (cases No. 40,59,84,26,74). Of the seven patients with a duration of terminal symptoms of seconds to a few minutes (instantaneous death), four (cases No. 82,40,59,26) only had uniform ventricular ectopic beats on the final monitoring.

At the time of the final monitoring, seven of the 12 patients were receiving digoxin, while three were being treated with a drug having an antiarrhythmic effect: beta-blocker (case No. 82), quinidine (case No. 58) and verapamil (case No. 49).

Figure 11 shows that there was no progression in the pattern of arrhythmias prior to death. The six-month monitoring was of no prognostic value in the seven patients who died suddenly later than six months after the infarction (table 30). Table 31 shows the ventricular arrhythmias during 24-hour tape-recording in the late hospital phase in the 20 patients with a major cardiac event (re-infarction, sudden or non-sudden cardiac death) as compared to the remaining patients. The occurrence of multiform ventricular ectopic beats and ventricular ectopic beats as bigeminy were significantly more frequent in patients with a major cardiac event ($P < 0.01$).

Table 30

Ventricular arrhythmias during tape-recording six months after the infarction in relation to sudden cardiac death in the subsequent follow-up period.

	Patients who died suddenly (n=7)	Patients who survived (n=84)
Any VEB	7 (100%)	76 (90%)
Multiform VEB	1 (14%)	23 (27%)
Paired VEB	2 (29%)	15 (18%)
RonT VEB	0 (0%)	1 (1%)
Ventricular tachycardia	0 (0%)	6 (7%)
Bigeminy	4 (57%)	20 (24%)
Mean VEB > 1 per 100 QRS	1 (14%)	5 (6%)

Table 31

Ventricular arrhythmias during tape-recording in the late hospital phase in relation to cardiac events (re-infarction, cardiac death) during an average follow-up period of 18 months.

	Patients with cardiac event (n=20)	Patients alive without cardiac event (n=79)*
Any VEB	19 (95%)	71 (90%)
Multiform VEB	9 (45%)**	12 (15%)
Paired VEB	3 (15%)	11 (14%)
RonT	1 (5%)	2 (3%)
Ventricular tachycardia	2 (10%)	1 (1%)
Bigeminy	7 (35%)**	7 (9%)
Mean VEB > 1. per 100 QRS	5 (25%)	25 (32%)

* one patient with non-cardiac death excluded

** $p < 0.01$

DISCUSSION

In early investigations from coronary care units, the occurrence of fatal ventricular arrhythmias was said to be preceded by particular types of ventricular ectopic beats, the so-called "warning arrhythmias" (Julian et al. 1964, Lown et al. 1967). At almost the same time, epidemiological studies showed that the presence of ventricular ectopic beats on a resting electrocardiogram (Chiang et al. 1969) and during 6-hour electrocardiographic tape-recording (Hinkle et al. 1969) were related to an increased risk of sudden cardiac death, even though other investigators were unable to find any individual prognostic importance of ventricular ectopic beats (Fisher & Tyroler 1972, Crow et al. 1975). The Coronary Drug Project (1973) showed that the occurrence of ventricular ectopic beats per se on the resting electrocardiogram in postinfarction patients was related to an increased risk of sudden cardiac death. It had been assumed that the presence of ventricular ectopic beats is an expression of electrical instability in the myocardium (Lown et al. 1975), and that this instability is a permanent or progressive condition which could be employed as an important prognostic indicator, even after the acute phase of a myocardial infarction.

In recent years some doubt has been cast on the existence of warning arrhythmias during the acute phase of an infarction (Lie et al. 1975, El Sherif et al. 1976, de Soyza et al. 1979), and only a few investigators have found the occurrence of ventricular arrhythmias in the first days of an in-

farction to be of any important long-term prognostic value (Sloman & Prineas 1973). Interest has therefore been concentrated on evaluation of the relationship between ventricular arrhythmias during the late hospital phase and subsequent cardiac death, the latter being considered an arrhythmia death (Bleifer et al. 1974, Liberthson et al. 1974, Lown et al. 1975, Haghfelt 1976, Julian 1976, Gradman et al. 1977, Pool et al. 1978).

At present there are several such investigations using electrocardiographic tape-recording of varying duration (Moss et al. 1971, Kotler et al. 1973, Van Durme 1975, Vis-mara et al. 1975, Moss et al. 1977, Schulze et al. 1977, Federman et al. 1978, Rehnqvist et al. 1978). The studies are, as the present, first and foremost characterized by a small number of patients with sudden cardiac death (4-17 cases) and, with the exception of Federman et al. (1978), by finding a significant relationship between the number of complicated forms of ventricular arrhythmias and sudden cardiac death. However, it has not been possible, based on these investigations, to employ the pattern of ventricular ectopic beats in clinical work for the identification of well-defined high risk groups.

The present investigation demonstrates some of the difficulties in selecting high risk groups, as sudden cardiac death frequently occurred shortly after a 24-hour tape-recording showing only a few uniform ventricular ectopic beats. At the same time, the present investigation shows

that complicated ventricular arrhythmias are an extremely frequent finding in postinfarctional patients, when the monitoring has a duration of 24 hours and the electrocardiographic analysis is carried out by means of an arrhythmia computer. This means that ventricular arrhythmias detected by the various types of monitoring and analysis systems can play a different prognostic role. Further, that even if complicated ventricular arrhythmias are significantly associated with sudden cardiac death, this observation is of limited practical value.

The fact that ventricular ectopic beats have a prognostic importance per se is undoubtedly correct, based on the two extensive investigations (Ruberman et al. 1977, Moss et al. 1979). In their very recently published study, Moss et al. (1979) carried out 6-hour monitoring of 940 patients below the age of 66 years during the late hospital phase of a myocardial infarction. Fifty-five cases of sudden cardiac death (duration of symptoms less than one hour) and 43 cases of non-sudden cardiac death occurred during an average follow-up period of 36 months (range 1-60 months). Complicated ventricular arrhythmias were present in only 27% of the patients and were found, independent of a large number of clinical variables, to carry prognostic information for both sudden and non-sudden cardiac death. Figure 12A demonstrates, however, the considerable dilemma in which the clinician stands with regard to treatment. Provided an attempt is made to carry out antiarrhythmic intervention

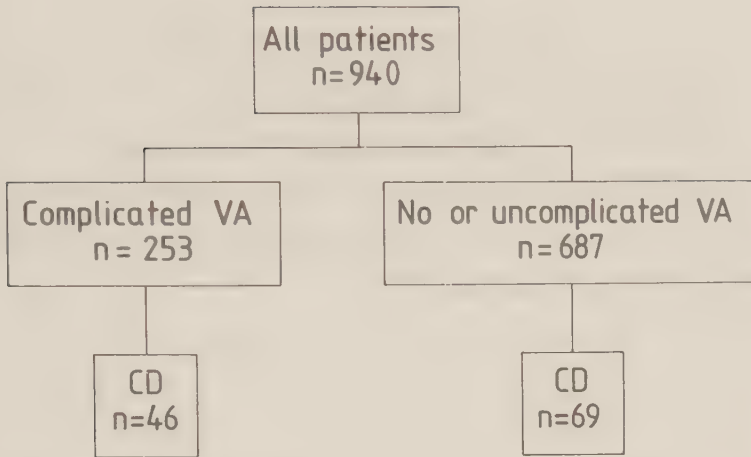


Figure 12 A

Association between ventricular arrhythmias (VA) in late hospital phase and cardiac death (CD) during a mean follow-up period of 36 months (range 1-60 months).

Modified from Moss et al. (1979).

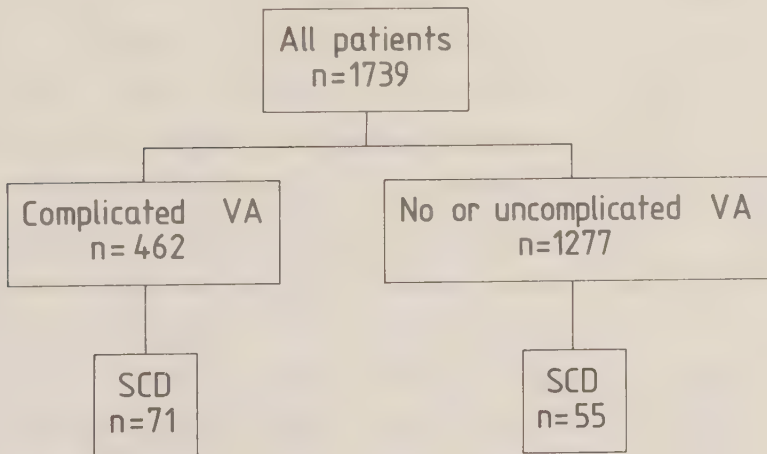


Figure 12 B

Association between ventricular arrhythmias (VA) in postinfarction patients and the age-adjusted risk of sudden cardiac death (SCD).

Modified from Ruberman et al. (1977).

based on the pattern of arrhythmias, one will in the group with complicated arrhythmias treat many patients who apparently are doing well, but what is more important, a considerable number of patients suffering from sudden cardiac death despite uncomplicated ventricular ectopic beats will not be given treatment.

Figure 12B shows the results of the investigation of Ruberman et al. (1977) including 1739 male postinfarctional patients each studied using a single monitoring of one hour at varying times (at least 3 months) after the infarction. The stated occurrence of sudden cardiac death is the predicted, age-corrected, 3-year value, and figure 12B illustrates the same treatment dilemma as mentioned above.

Among a number of other factors, the difference in the evaluation of the prognostic importance of the pattern of ventricular arrhythmias can be due to a difference in the definition of sudden cardiac death. The present investigation employs a duration of symptoms of less than 24 hours, Vismara et al. (1975) use a maximum of six hours, Rehnqvist et al. (1978) a maximum of two hours, while the majority define sudden cardiac death as having a duration of symptoms of less than one hour (Chiang et al. 1969, Coronary Drug Project Research Group 1973, Fisher & Tyroler 1973, Van Durme 1975). Federman et al. (1978) do not state any definition, while Ruberman et al. (1977) use the term sudden cardiac death defined as "those occurring within minutes of a patient's usual state of health in the absence of symptoms or

findings suggesting acute myocardial infarction". There is hardly any doubt that a definition as mentioned last, will definitely focus on the primary arrhythmia deaths. In the present investigation the patients with terminal symptoms of a duration of seconds or a few minutes do not differ with regard to the arrhythmia pattern from the remaining patients. In agreement with this ventricular ectopic beats had the same prognostic value with regard to the prediction of both sudden (within one hour) as non-sudden cardiac death in the investigation of Moss et al. (1979).

The present study does not suggest that repeated monitoring will increase to any great extent the possibility of predicting sudden cardiac death in the individual patient. This must be seen on the background of the arrhythmia pattern, as stated on page 68, varying considerably from monitoring to monitoring in the individual patient, inasmuch as only 19 patients had uncomplicated ventricular arrhythmias at all the monitorings, and only six entirely complicated ventricular arrhythmias. None of the patients suffering sudden cardiac death belonged to these two groups. A few other investigations include repeated monitorings. Moss et al. (1977) found that the pattern of arrhythmias during the late hospital phase only had a significant prognostic importance during the first four months after the infarction, but not for the first 12 months. Renewed monitoring five months after the infarction was not of progno-

stic value for the following seven months.

In contrast to this, Rehnqvist et al. (1978) state that the occurrence of complicated ventricular arrhythmias during repeated 6-hour telemetry 12 months after the primary infarction were of prognostic importance for the following year. Patients who had complicated ventricular arrhythmias in both the late hospital phase as well as one year later had a particularly unfavourable course. The total number of cases of sudden cardiac death was 16 during the follow-up period of two years.

The problems of using the pattern of ventricular arrhythmias for identifying high risk groups have been emphasized during later years by several reports demonstrating that the occurrence of ventricular tachycardia, both in the postinfarction patients (Anderson et al. 1978, de Souza et al. 1978, Møller et al. 1980) and in patients with various types of heart disease (Winkle et al. 1977) is usually related to a good prognosis.

It would therefore be desirable to supplement the monitoring with other methods in order to be able to classify patients more precisely from the prognostic point of view, and not least with regard to factors which may be influenced by treatment. Further, it would be desirable to identify parameters which can comparatively simply be determined by non-invasive methods.

Thus it has been emphasized by Schulze et al. (1977) that in patients with a left ventricular ejection fraction of

less than 40%, determined by gated blood pool scanning, the occurrence of complicated ventricular arrhythmias was the factor indicating patients with a poor or better prognosis. It is possible that the motion pattern of the left ventricle and the ejection fraction determined by echocardiography together with the occurrence of ventricular arrhythmias determined by long-term electrocardiographic tape-recording can contribute to this, particularly as invasive methods, such as coronary arteriography and ventriculography are hardly reasonable to carry out in the large majority of patients. Right-sided heart catheterization with programmed electrical stimulation and registration of the repetitive ventricular response (Greene et al. 1978) requires special experience and at present is not well-suited for screening patients.

The problem of evaluating the therapeutical consequences will still exist. It has been postulated that beta-blocker treatment can prevent sudden cardiac death in postinfarctional patients (Wilhelmsen et al. 1974, Multicentre International Study 1975, Andersen et al. 1979), but the mode of action is still unknown, and the investigations available do not include long-term monitoring. Such monitoring will possibly improve the classification of the patients into sub-groups liable to benefit from treatment. Thus there is still a considerable amount of work to be done in identifying high risk groups and to study the effect of intervention trials.

SUMMARY

In an average follow-up period of 18 months (range 15-22 months) one case of non-cardiac death, two cases of non-sudden and 12 cases of sudden cardiac death occurred. Further there were nine cases of non-fatal reinfarction. A total of 20 patients had re-infarction and/or cardiac death. A comparison of the patterns of ventricular ectopic beats during 24-hour electrocardiographic tape-recording in the late hospital phase showed that multiform ventricular ectopic beats occurred significantly more frequently in the 12 patients suffering sudden cardiac death than in the 85 patients alive at the time of follow-up ($P < 0.05$). No significant difference was found with regard to the other types of ventricular ectopic beats. The pattern of arrhythmia at night was of no prognostic value.

Monitoring six months after the infarction was not predictive with regard to subsequent cardiac death.

A total of eight cases of sudden cardiac death occurred after the latest monitoring had only demonstrated uniform ventricular ectopic beats. No progression was observed from monitoring to monitoring before sudden cardiac death. No difference was found in the pattern of arrhythmias between patients with terminal symptoms of a duration of seconds and hours, respectively. The medicament treatment had no influence on this.

The pattern of ventricular arrhythmias during the late hospital phase showed that multiform ventricular ectopic beats as well as ventricular ectopic beats as bigeminy were signi-

ificantly more frequent in patients with subsequent cardiac death and/or re-infarction ($P < 0.01$).

Based on the fact that the majority of patients showed complicated ventricular arrhythmias it is concluded that the pattern of ventricular arrhythmias during 24-hour electrocardiographic tape-recording did not permit a clinically employable identification of high risk groups with regard to sudden cardiac death. The absence of complicated ventricular arrhythmias did not identify a low risk group.

CHAPTER VIII : VENTRICULAR ARRHYTHMIAS AND HEART
RATE IN PERSONS WITHOUT APPARENT
HEART DISEASE

At the time at which the present investigation was planned, little knowledge was available as to the occurrence of arrhythmias during tape-recording of persons without apparent heart disease (Gilson 1965, Hinkle et al. 1969). The studies employed a short period of monitoring during daytime hours, and analysis without computer assistance. Therefore it was decided to study a group of normal subjects having a similar age distribution to the postmyocardial infarction group, employing the equipment described in this investigation.

RESULTS

The investigation comprises 24 men between the age of 40 to 65 years (mean 53 years) without signs of heart disease. These comprised six pairs of monozygotic and six pairs of

dizygotic twins from the Danish twin register (Hauge et al. 1968), initially selected in order to study the genetic influence on heart rate and ventricular arrhythmias. As the heart rate, in contrast to the ventricular ectopic activity, was found to be partly genetically determined (unpublished data), the results should be evaluated taking this into consideration. The following criteria were employed for inclusion in the study: 1) no cardiac complaints in the medical history, 2) normal blood pressure, 3) normal heart stethoscopy, 4) normal resting electrocardiogram (12 leads) (ventricular arrhythmias not included in the criteria), 5) normal heart size on the X-ray of the chest, 6) no ischaemic changes on the electrocardiogram during maximal exercise testing (bicycle ergometer) and 7) no drug therapy.

Each person was subjected to approximately 24 hours of ambulatory electrocardiographic recording. The period 0 to 6 a.m. was included in all these and the recording usually commenced between 3 and 4 p.m.. Normal daily activity was continued during the monitoring. Each tape was analyzed as described in chapter II.

None of the persons were found to have ventricular ectopic beats on the 60 sec resting electrocardiogram. As can be seen from table 32, the average heart rate/min on the resting electrocardiogram was 66 ± 10 (SD) and significantly slower than for the postinfarction patients ($P < 0.001$).

The average monitoring time was 21 hours and thus slightly shorter and in addition of somewhat more varying length than in the postmyocardial infarction group. The average heart rate/min during monitoring was 78 ± 9 (SD) and not different from that of the postmyocardial infarction patients. Ventricular ectopic beats occurred during monitoring in 11 (46%) against 90 - 91% in the postmyocardial infarction group ($P < 0.001$). Three persons (13%) had multiform ventricular ectopic beats, while repetitive ventricular ectopic beats or R on T did not occur. These findings were observed in 34-50% of the post-myocardial infarction patients ($P < 0.05$). An average number of ventricular ectopic beats exceeding 1/hour was found in two persons, against 51-67% of the post-myocardial infarction patients. The diurnal variation pattern is shown in table 33. The average heart rate during the period of sleep (0 - 6 a.m.) was significantly slower in the reference group than in the postmyocardial infarction patients in respect of the investigations in the late hospital phase and the first posthospital control ($P < 0.05$), while the heart rate during the day time was most rapid in the reference group. Thus it can be seen that the difference in the heart rate during night and day was considerably greater in the reference group than in postmyocardial infarction patient. The occurrence of ventricular ectopic beats shows, as in postmyocardial infarction patients, a rather uncharacteristic diurnal variation with an insignificant reduction at night.

Table 32

Heart rate and ventricular ectopic beats during 24-hour electrocardiographic tape-recording in 24 men between the age of 40-65 years and without apparent heart disease.

Resting electrocardiogram

Mean heart rate (min^{-1})

mean	66
SD	10
range	46-79

Ventricular arrhythmias

No. with VEB present	0
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Electrocardiographic tape-recording

Duration of monitoring (min.)

mean	1275
SD	199

Mean heart rate (min^{-1})

mean	78
SD	9
range	57-91

Ventricular ectopic beats

No. with VEB present	11
No. with multiform VEB	3
No. with mean VEB > 1 (hour^{-1})	2
No. with mean VEB > 10 (hour^{-1})	1
mean VEB (hour^{-1}), range	0-33
mean VEB (10.000 QRS^{-1}), range	0-63

Table 33

Diurnal variation of heart rate and ventricular ectopic beats during 24-hour electrocardiographic tape-recording in 24 men between the age of 40-65 years and without apparent heart disease.

Parametre	Period of monitoring			
	0-6 a.m. (n=24)	6-12 a.m. (n=23)	12-6 p.m. (n=23)	6-12 p.m. (n=24)
Duration of monitoring (min)				
mean	359	308	277	360
SD	6	101	90	0
Mean heart rate (min^{-1})				
mean	63	85	91	80
SD	8	13	10	10
range	49-78	61-110	77-113	59-103
Ventricular ectopic beats				
No. with VEB present	5	10	8	6
No. with multiform VEB	0	2	2	0
No. with mean VEB $> 1(\text{hour}^{-1})$	3	2	2	4
No. with mean VEB $> 10(\text{hour}^{-1})$	1	1	1	1
mean VEB (hour^{-1}) range	0-28	0-62	0-18	0-19
mean VEB (10.000 QRS $^{-1}$) range	0-65	0-111	0-30	0-36

DISCUSSION

The present investigation demonstrates that there is a considerable difference in respect of both heart rate and the occurrence of ventricular ectopic beats between a group of middle aged men without signs of heart disease and a group of almost similarly aged postmyocardial infarction patients. Table 34 gives a survey of previously published reports concerning persons without apparent heart disease.

In the study of Brodsky et al. (1976) it was found, following 24 hours of monitoring of 50 male students between the age of 23 and 27 years, that the average heart rate/min was 73 ± 7 (SD) for the monitoring as a whole and 56 ± 6 (SD) during sleep. The frequencies were significantly slower than in the reference material presented here ($P < 0.05$, $P < 0.01$, respectively).

The difference probably results from a better physical condition in the male students, but the heart rate of the total period of monitoring could also have been influenced by the fact that the students in Brodsky's study presumably mainly had sedentary work, while about half of the persons in the present investigation had manual work. Other factors may have played a part, as Clarke et al. (1976) during 48 hours of monitoring of 86 clinically healthy persons between the age of 16 and 65 years, found a significantly more rapid heart rate among smokers as compared to those who did not smoke. The exact heart rate is not stated in the report, but it was independent of age and more

Table 34

Ventricular arrhythmias and heart rate during electrocardiographic tape-recording in persons without apparent heart disease. A comparison with previous studies.

Authors	Number of persons	Age (years)	Duration of monitoring	Per cent with VEB present	Per cent with complicated VEB	heart rate/min mean $\pm$ SD
Hinkle et al. 1969	283	mean 55	6 h	62	19	-
Clarke et al. 1976	86	16-65	48 h	73	12	-
Kennedy & Underhill 1976	25	35-65	48 h	35	13	
Raftery & Cashman 1976	53	20-75	24 h	17	2	
Brodsky et al. 1977	50	23-27	24 h	50	22	73 $\pm$ 7
Rehnqvist & Sjögren 1977	25	mean 60	6 h **	24	8	-
Federman et al. 1978	21	40-60	24 h	48	10	-
Present study	24	40-65	24 h	46	13	78 $\pm$ 9

* 58 persons had ischaemic heart disease

** telemetry

rapid in women than in men. The latter observation has not been confirmed in the postmyocardial infarction patients studied here, but has been found by others in normal subjects (Bjerregård, personal communication 1979). In the work of Gilson (1965), mentioned in the beginning of this chapter, it was found that only two of 37 persons without apparent heart disease showed "what seemed to be an unusual number of ventricular ectopic beats" during five hours of electrocardiographic monitoring performed one time in each of four consecutive years.

The investigations in table 34 are inhomogenous, both with regard to materials and methods, and the material presented by Hinkle et al. (1969) includes about twenty per cent heart disease. In the work of Brodsky et al. (1976) both echocardiographic examination as well as exercise electrocardiography were employed to exclude heart disease, while the other investigators used the medical history, clinical examination, and in the majority of cases, resting electrocardiogram, blood pressure and X-ray of the chest. The age distribution of the persons in the work of Hinkle et al. (1969), Rehnqvist & Sjögren (1977), Federman et al. (1978), is more or less as in the present investigation. The duration of the investigations varies from 6 to 48 hours of telemetry or tape recording carried out during admission to hospital or as outpatient examination. Table 34 shows a pronounced variation in the occurrence of ventricular ectopic beats from investigation to inve-

stigation. The high incidence in the study of Clarke et al. (1976) could be based on the use of a monitoring period of 48 hours, even though the day to day variation is not known in persons without signs of heart disease. The high incidence also seen in the investigation of Hinkle et al. (1969) results, presumably, from the investigation including persons with heart disease.

The low incidence in the work of Raftery & Cashman (1976) in contrast to the high incidence among the students of Brodsky et al. (1976) cannot be easily explained, but perhaps results from the use of simple analytic equipment in the former investigation with the subsequent risk of false negative findings.

The stated occurrence of complicated ventricular arrhythmias shows a somewhat smaller variation. The term complicated ventricular ectopic beats is employed in the majority of investigations for multiform and repetitive ventricular ectopic beats, as well as R on T phenomenon. In the work of Hinkle et al. (1969) the term also includes patients with ventricular ectopic beats as bigeminy and trigeminy, while multiform ventricular ectopic beats are apparently not included. In the study of Clarke et al. (1976) the material includes persons with an average of more than five ventricular ectopic beats/hour (7 persons) during the 48 hours of monitoring. The highest average number of ventricular ectopic beats per hour were with Clarke et al. (1976) 59, while one patient of Brodsky et al. (1976) had on average more than 50 per hour. While the more advanced

types of ventricular ectopic beats did not occur in the present study, Clarke et al. (1976) found two cases of ventricular tachycardia and two cases of R on T in four different persons. Brodsky et al. (1976) observed three cases of R on T and one case of ventricular tachycardia. Federman et al. (1978) and Rehnqvist & Sjögren (1977) found no cases of paired ventricular ectopic beats, R on T or ventricular tachycardia, and the patients with complicated ventricular ectopic beats all had multiform ventricular ectopic beats. While Hinkle et al. (1969) observed an increasing occurrence of ventricular ectopic beats with age, no such observation was made by Clarke et al. (1976). The material presented here is too small for an evaluation of this.

Summarizing, it can be said that the information available on the occurrence of ventricular ectopic beats in apparently healthy persons is still confusing, but that the three studies containing a comparison of postmyocardial infarction patients and normal subjects (Rehnqvist & Sjögren 1977, Federman et al. 1978, present study) all demonstrate a significantly higher frequency in post-myocardial infarction patients of both "any" ventricular ectopic beats and complicated ectopic beats, even though the findings in the individual person overlap between the two groups.

Finally, it should be mentioned that in the present investigation, sudden cardiac death occurred in several postmyocardial patients one day to a few weeks after 24-

hours of electrocardiographic monitoring showing a ventricular arrhythmia pattern which did not differ from that observed in the reference group.

SUMMARY

A reference material was studied consisting of 24 men without signs of cardiac disease and of similar age to the postmyocardial infarction patients. The average heart rate on the resting electrocardiogram was significantly slower than that of the postmyocardial infarction patients ($P < 0.05$), while no difference was found with regard to the total electrocardiographic monitoring. None of the reference persons had ventricular ectopic beats on the resting electrocardiogram, whereas 11 (46%) had ventricular ectopic beats during monitoring, against 90-91% of the postmyocardial infarction patients ($P < 0.001$). Three of the reference group had multiform ventricular ectopic beats, while repetitive types and R on T phenomena did not occur. The average number of ventricular ectopic beats per 10,000 QRS complexes varied from 0 to 63. Thus there is overlapping between the reference group and the postmyocardial infarction patients, both in respect of quantity and quality. It is particularly interesting to note that several cases of sudden cardiac death occurred in the postmyocardial infarction patients within days to a few weeks after the monitoring with an arrhythmia pattern, which did not differ from that observed in persons without apparent signs of heart disease.

CHAPTER IX : SUMMARY AND GENERAL CONCLUSIONS

The object of the present investigation has been to describe the course of ventricular arrhythmias during the first six months following an acute myocardial infarction, to determine the diurnal variation of ventricular ectopic beats, to evaluate the relationship between arrhythmias and a number of clinical parametres and finally to throw some light on the usefulness of the pattern of ventricular arrhythmias for the selection of high risk groups with regard to sudden cardiac death.

The investigation includes 100 consecutive patients below the age of 70 years discharged alive from the coronary care unit of the Odense University Hospital following admission for definite acute myocardial infarction. The patients were treated in accordance with the usual principles of the department. Taking due regard to the age criteria, the patients were found to be representative of the infarction population as a whole.

One of the last days prior to discharge a 60 second resting electrocardiogram (12 leads) was recorded, and immediately thereafter a 24-hour electrocardiographic tape-recording (2 leads) commenced, using a small portable tape-recorder. These registrations were repeated approximately one, three and six months after the infarction. The tape recordings thus obtained were analysed at 60 times real time by means of an arrhythmia computer. Follow-up was carried out on average 18 months (range 15-22 months) after the infarction.

Ventricular ectopic beats occurred in approximately 90% of the patients during the individual monitorings, and only two patients were completely free from ventricular ectopic beats during all tape-recordings. Complicated ventricular arrhythmias (multiform, repetitive, R on T) occurred in 34%, 51%, 41% and 39% of the patients on the four occasions. Thus a significant progression took place in connection with discharge from hospital. This means that the pattern of ventricular arrhythmias during the late hospital phase was not representative for the posthospital period. For the four monitorings as a whole, multiform ventricular ectopic beats occurred in 70%, paired ventricular ectopic beats in 47%, R on T phenomenon in 9% and ventricular tachycardia in 19% of the patients. The incidence of these types of arrhythmias was closely correlated to the number of ventricular ectopic beats. No clear relationship was found between the pattern of arrhythmias

and the medicament treatment.

The results indicate that the duration of antiarrhythmic treatment should include at least the first six months after the infarction.

In order to evaluate the diurnal variation of ventricular arrhythmias the 24 hours of monitoring were divided into four six-hour periods commencing at midnight. The occurrence of complicated ventricular arrhythmias showed no significant diurnal variation, but there was a tendency to a higher frequency from 12 to 6 p.m. and a lower from 0 to 6 a.m.. At the three posthospital monitorings the average number of ventricular ectopic beats per hour was significantly lower at night than during the rest of the day. No significant diurnal variation was observed after correction for differences in heart rate, thus suggesting a relationship between heart rate and the number of ectopic beats.

A closer analysis of the 65 tapes with more than 600 ventricular ectopic beats/day showed that the number of ventricular ectopic beats (corrected for heart rate) increased at night in about 25% of the patients and was reduced by at least 75% in almost one half of the patients. A large reduction in heart rate at night was accompanied by an extraordinary large reduction in the number of ectopic beats, indicating that factors other than the heart rate itself play a role - presumably the magnitude of the sympathetic tone and severity of the underlying heart disease.

se. Beta-blocker treatment would be logical in patients with a good correlation between heart rate and the number of ventricular ectopic beats. However, as the diurnal variation was not reproducible from tape to tape in the individual patient, this makes the selection of a suitable antiarrhythmic drug more complicated.

The occurrence of ventricular arrhythmias was independent of a number of conventional risk factors. In the late hospital phase, but not during the posthospital period, age above 60 years and pre-admission angina pectoris or congestive heart failure were associated with an increased frequency of complicated ventricular arrhythmias. For the monitorings as a whole, an increased incidence of arrhythmias was observed in patients with left heart failure in the coronary care unit, as well as in patients with transmural infarctions, pointing to a relationship between extent of myocardial injury and occurrence of ventricular arrhythmias.

Evaluated on the basis of the measured maximum enzyme activities in serum, the extent of myocardial damage played an increasing role throughout the period of follow-up. So that six months after the infarction a significant relationship was observed between both the qualitative and quantitative patterns of arrhythmia and the maximum enzyme activity in the coronary care unit.

Two cases of non-sudden and 12 cases of sudden cardiac death occurred in the average follow-up period of 18 months (range 15-22 months). There were nine cases of non-fatal re-infarction. A total of 20 patients suffered a re-infarction and/or cardiac death.

In the late hospital phase, the frequency of the various types of ventricular arrhythmias was higher in the 12 patients with sudden cardiac death than in the 85 patients alive at the time of follow-up, but only with regard to multiform ventricular ectopic beats was a significant difference observed. No progression was seen from monitoring to monitoring prior to the fatal episode; thus sudden cardiac death occurred in eight patients after the latest monitoring had shown uniform ventricular ectopic beats only.

Ventricular ectopic beats as bigeminy or from more than one focus were, with monitoring during the late hospital phase, significantly more frequent in patients with subsequent cardiac death and/or re-infarction.

The monitoring six months after the infarction was of no prognostic importance with regard to subsequent death.

It is concluded that the pattern of ventricular arrhythmias did not permit a selection of high risk groups. At the same time, it should be noted that the absence of complicated ventricular ectopic beats does not identify a low risk group.

In connection with the investigation, 24-hour ambulatory electrocardiographic monitoring of 24 men between the ages of 40-65 years, without apparent heart disease was carried out. Ventricular ectopic beats occurred in 11 persons (46%), in three as complicated types. In both cases significantly less frequently however, than in the postinfarction patients.

GENERAL CONCLUSIONS

1. Ventricular ectopic beats occur in all postinfarction patients, in the great majority as complicated types. The pattern of ventricular arrhythmia progresses significantly in connection with discharge and is, six months after the infarction, still more pronounced than during the late hospital phase. Any antiarrhythmic treatment therefore should include at least the first six months after the infarction.
2. The various qualitative types of ventricular arrhythmias show no significant diurnal variation. In about 75% of the patients the number of ventricular ectopic beats is reduced at night. The pattern of circadian variation is not reproducible in the individual patient, and is thus difficult to employ for the selection of a suitable antiarrhythmic drug.
3. The investigation suggests that the extent of the myocardial injury is the factor playing the greatest role with regard to the occurrence of ventricular

arrhythmias during the posthospital phase of a myocardial infarction.

4. The pattern of ventricular arrhythmias does not permit, even following repeated 24-hour tape-recording, an identification of well-defined high or low risk groups in respect of the occurrence of sudden cardiac death.
5. The present investigation demonstrates that ventricular arrhythmias are significantly more frequent in postinfarction patients than in similarly aged men without apparent heart disease.

KAPITEL X : RESUME OG GENERELLE KONKLUSIONER

Undersøgelsens formål har været at beskrive forløbet af ventrikulære arytmier det første halve år efter et akut myokardieinfarkt, at belyse det ventrikulære ekstrasystolimønsters døgnvariation, at vurdere sammenhængen mellem arytmiforekomsten og en række kliniske parametre samt endelig at belyse det ventrikulære arytmi-mønsters anvendelighed til udpegning af højrisikogrupper med hensyn til pludselig kardial død.

Undersøgelsen omfatter 100 konsekutive patienter under 70 år udskrevet i live efter indlæggelse i medicinsk afdeling B, Odense sygehus for sikkert akut myokardieinfarkt. Alderskriteriet taget i betragtning, fandtes patienter ikke at adskille sig fra infarktpopulationen som helhed.

En af de sidste dage før udskrivelsen blev optaget et 60 sekunder langt hvile-elektrokardiogram (12 afledninger), og i umiddelbart tilslutning hertil foretaget 24-timers elektrokardiografisk monitorering (2 afledninger), ved hjælp af en lille bærbar båndoptager. Undersøgelsesprogrammet blev gentaget cirka én, tre og seks måneder efter infarkt-et. De foretagne båndoptagelser blev analyseret med 60 gange indspilningshastigheden ved hjælp af en arytmicomputer. Gennemsnitlig 18 måneder (variationsbredde 15-22 måneder) efter infarkt blev foretaget opfølgning af patienterne.

Ventrikulære ekstrasystoler forekom hos omkring 90% af patienterne ved den enkelte monitorering, og kun to patienter var helt uden ventrikulære ekstrasystoler under monitoreringerne som helhed.

Komplicerede ventrikulære arytmier (multiforme, repetitive, R på T) forekom hos 34%, 51%, 41% og 39% af patienterne ved de fire monitoreringer. Der forekom således en signifikant progression i det ventrikulære arytmi-mønster i forbindelse med udskrivelsen. Dette betyder, at arytmi-forholdene i den sene hospitale fase ikke er repræsentative for den post-hospitale periode. For de fire monitoreringer som helhed forekom multiforme ventrikulære ekstrasystoler hos 70%, parvise hos 47%, R på T hos 9% og ventrikulær takykardi hos 19% af patienterne. Forekomsten af disse arytmi-former var nært korreleret til antallet af ventrikulære ekstrasystoler.

Der fandtes ingen tydelig sammenhæng mellem arytmimønstret og den medikamentelle behandling.

Undersøgelsen tyder på, at varigheden af en eventuel anti-arytmisk behandling bør omfatte mindst de første seks måneder efter infarkt.

Til vurdering af de ventrikulære arytmiers døgnvariation inddeltes døgnet i fire 6-timers perioder, startende ved midnat. Forekomsten af komplicerede ventrikulære arytmier viste ingen signifikant døgnvariation, men en tendens til den største hyppighed i tidsrummet 12-18 og den laveste fra midnat til klokken 6 om morgenen. Ved de tre posthospitale monitoreringer var det gennemsnitlige antal ventrikulære ekstrasystoler/time signifikant lavere om natten end i den øvrige del af døgnet. Efter korrektion for forskelle i hjerterefrekvens i de to tidsrum fandtes ingen signifikant døgnvariation, hvilket tyder på en sammenhæng mellem hjerterefrekvens og antallet af ekstrasystoler. En nøjere analyse af de 65 bånd med mere end 600 ventrikulære ekstrasystoler/dag viste, at antallet af ventrikulære ekstrasystoler tiltog om natten hos omkring 25% af patienterne og reduceredes med mindst 75% hos knapt halvdelen. En stor natlig reduktion i hjerterefrekvens var ledsaget af en ekstraordinær stor reduktion i antallet af ekstrasystoler tydende på, at andre faktorer end hjerterefrekvens i sig selv spiller en rolle - formentlig graden af sympatisk tonus og omfanget af den underliggende hjertesygdom. Fra et praktisk synspunkt ville beta-blokker-behandling være logisk

hos patienter med en god korrelation mellem hjertefrekvens og antallet af ventrikulære ekstrasystoler, men døgnvariationsmønstret var ikke reproducerbart fra bånd til bånd hos den enkelte patient.

Forekomsten af ventrikulære arytmier var uafhængig af en række konventionelle risikofaktorer. I den sene hospitale fase, men ikke i den posthospitale periode, var alder over 60 år samt angina pectoris og kongestiv hjersteinsufficiens forud for indlæggelsen forbundet med en øget forekomst af komplicerede ventrikulære arytmier. For monitoreringerne som helhed fandtes en øget arytmiforekomst hos patienter med kongestiv hjersteinsufficiens i koronarafsnittet og hos patienter med transmurale infarkter tydende på en sammenhæng mellem myokardiebeskadigelsens omfang og arytmiforekomsten. Vurderet på basis af de målte maksimale enzymaktiviteter i den akutte fase spillede infarktstørrelsen en tiltagende rolle gennem opfølgningsperioden. Seks måneder efter infarkt fandtes signifikant sammenhæng mellem såvel det kvalitative som det kvantitative arytmimønster og den målte maksimale enzymaktivitet i koronarafsnittet.

I en gennemsnitlig opfølgningsperiode på 18 måneder (variationsbredde 15-22 måneder) forekom to tilfælde af ikke-pludselig og 12 tilfælde af pludselig hjertedød (symptomvarighed mindre end 24 timer). Der var ni tilfælde af ikke-dødeligt re-infarkt. I alt 20 patienter havde re-infarkt

og/eller død af kardial årsag.

I den sene hospitale fase var forekomsten af de forskellige former for ventrikulære arytmier hyppigere hos de 12 patienter med pludselig hjertedød end hos de 85 patienter, som var i live på opfølgningstidspunktet, men kun med hensyn til multiforme ventrikulære ekstrasystoler var forskellen signifikant. Der sås ingen progression fra monitorering til monitorering forud for den fatale begivenhed, således indtrådte pludselig hjertedød hos otte patienter efter at den senest foretagne monitorering alene havde vist uniforme ventrikulære ekstrasystoler.

Ventrikulære ekstrasystoler som bigemini eller fra mere end ét focus var ved monitoreringen i den sene hospitale fase signifikant hyppigere hos patienter med efterfølgende kardial død eller re-infarkt. Monitoreringen seks måneder efter infarkt var ikke af prognostisk værdi for den resterende opfølgningsperiode.

Det konkluderes, at det ventrikulære arytmimønster ikke tillader udpegning af højrisikogrupper. Samtidig bemærkes, at fravær af komplicerede ventrikulære arytmier ikke identificerer en lavrisikogruppe.

I tilslutning til undersøgelsen blev foretaget 24-timers ambulant elektrokardiografisk monitorering af 24 mænd i alderen 40-65 år uden tegn til hjertesygdom. Ventrikulære ekstrasystoler forekom hos 11 personer (46%), hos tre personer i komplicerede former. I begge tilfælde således signifikant mindre hyppigt end hos postinfarktpatienterne.

Generelle konklusioner.

1. Ventrikulære ekstrasystoler forekommer hos alle postinfarktpatienter og hos de fleste i komplicerede former. Det ventrikulære arytmimønster progredierer signifikant i forbindelse med udskrivelsen og er seks måneder efter infarktets fortsat mere udtalt end i den sene hospitale fase. En antiarytmisk behandling bør derfor mindst omfatte de første seks måneder efter infarktets.
2. De forskellige kvalitative typer af ventrikulære ekstrasystoler viser ingen signifikant døgnvariation. Hos omkring 75% af patienterne reduceres antallet af ventrikulære ekstrasystoler om natten. Døgnvariationsmønstret er ikke reproducerbart hos den enkelte patient og kan således vanskeligt anvendes i forbindelse med valget af hensigtsmæssig antiarytmisk behandling.
3. Undersøgelsen tyder på at myokardiebeskadigelsens omfang er den faktor, som spiller den største rolle for forekomsten af ventrikulære arytmier i den posthospitale fase af myokardieinfarktets.
4. Det ventrikulære arytmimønster tillader, selv under gentagen 24-timers monitorering, ingen identifikation af veldefinerede højrisikogrupper med hensyn til forekomsten af pludselig kardial død.

5. Ventrikulære arytmier er signifikant hyppigere hos postinfarktpatienter end hos en jævnaldrende gruppe mænd uden tegn til hjertesygdom.

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